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Physiotherapy and Combined Cognitive-Behavioural Therapy for Patients with Chronic Pelvic Pain Syndrome: Results of a Non-randomized Controlled Feasibility Trial.

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Abstract

Objective: To explore feasibility of combining physio- and psychotherapy for patients with chronic pelvic pain syndrome (CPPS) and to obtain first insights into symptom changes.

Design: Prospective non-randomized controlled pilot study.

Setting: Tertiary care facility with a specialized interdisciplinary outpatient clinic for patients with CPPS.

Participants: A total of 311 patients was approached; 60 participated. Thirty-six patients were included in the intervention group (mean age ± SD 48.6 years ± 14.8; 52.8% female) and 24 in the control group (mean age ± SD 50.6 years ± 14.5; 58.3% female). Fourteen participants were lost to follow up.

Interventions: Participants were non-randomly allocated to the intervention group with two consecutive treatment modules (physiotherapy and cognitive behavioural therapy) with a duration of nine weeks each or to the control group (treatment as usual).

Main outcome measures: Feasibility was operationalized using eligibility, willingness to participate, drop-out, and satisfaction. Outcomes included change in health-related quality of life (primary), depression severity and pain (secondary).

Results: Although eligibility and willingness-to-participate rates were low, satisfaction of the participants in the intervention group was high and drop-out rates were low. Results indicated a small and non-significant intervention effect in health-related quality of life and significant effects regarding depression severity and pain.

Conclusions: The combination of physio- and psychotherapy for patients with CPPS seems to be potentially promising. However, a subsequent fully powered randomized controlled trial is needed.

Trial registration: German Clinical Trials Register (DRKS00009976) and ISRCTN (ISRCTN43221600).

Keywords: chronic pelvic pain syndrome, cognitive behavioural therapy, physiotherapy, interdisciplinary treatment, feasibility study

Article Summary

Strengths and limitations of this study

- First study examining the feasibility of combining physio- and psychotherapy in patients with chronic pelvic pain syndrome.
- Inclusion of both women and men acknowledging the affectedness of both sexes.
- Besides feasibility testing, several patient relevant outcomes were examined providing first insight into effect of the combined physio- and psychotherapy.
- A control group was utilised; however, allocation to the study arms was not randomized.

Introduction

Chronic pelvic pain syndrome (CPPS) is a common chronic pain condition with pain perceived in pelvis-related structures and organs without an apparent pathology for at least six months [1]. Worldwide, prevalence rates in the general population range from 4% to 26.6% in women [2, 3] and 2% to 18% in men [4, 5]. Several risk and contributing factors exist [6], but the aetiology of CPPS is still unclear [7].

Several treatment strategies including psychotherapeutic and physiotherapeutic approaches exist, yet for most of these programmes, a distinct benefit was not found [8-11]. The physiotherapeutic approach with the currently best evidence with respect to pain reduction and improvement in quality of life is manual trigger point therapy alone or in combination with active therapy elements [11]. As for psychotherapy, somatocognitive approaches which encourage body awareness and reflection on pain cognitions might be helpful in reducing pain as demonstrated in a randomized-controlled trial [10]. However, existing reviews demonstrated that the successful treatment of CPPS remains challenging and that single treatment strategies often fail to be satisfactory [9]. A combination of physio- and psychotherapy might be a promising approach in reducing symptoms and increasing quality of life [10], so that a multidisciplinary treatment approach is highly recommended [1, 8, 12]. Nonetheless, to the best of our knowledge, no study has tested the combination of physio- and psychotherapy.

Another argument for a combination of treatment modalities is the heterogeneity of symptoms among patients with CPPS. The spectrum includes urogenital, gastroenterological, and/or sexual dysfunction [13]. CPPS is also associated with myofascial [12, 14] and psychopathological symptoms as well as a decreased health-related quality of life [12, 15-20]. Furthermore, there seems to be a linkage between myofascial and psychosocial factors [14]. The primary aim of this study was to explore the feasibility and acceptability of combining physio- and psychotherapy in a common therapy approach for female and male patients with CPPS. Feasibility was operationalized in terms of satisfaction with the therapy, willingness-to-participate, reasons for refusing to participate and attendance rate. Furthermore, in order to estimate the effect size for future sufficiently powered randomized clinical trials, a preliminary assessment of the intervention effects was investigated exploratively.

Material and Methods

Study design

The study was based on the principles of a "cohort multiple randomized controlled trial" (cmRCT) proposed by Relton et al. [21] Participants were recruited from a specialized outpatient clinic for patients with CPPS based at the University Medical Centre Hamburg-Eppendorf. From August 2012 to December 2017, several studies were conducted within the

Interdisciplinary Research Platform Chronic Pelvic Pain Syndrome (CPPS) [11, 14-20, 22-24]. In the CPPS outpatient clinic, patients underwent multimodal diagnostic algorithm consisting of psychosomatic, physiotherapeutic, urologic, and gynaecologic assessments. Patients signed informed consent, which allowed the contact for this study. The protocol for the study was published [23] and the study was registered at the German Clinical Trials Register (DRKS00009976) and at ISRCTN (ISRCTN43221600). Ethical approval for the CPPS outpatient clinic and for the feasibility study was given by the Ethics Committee of the Medical Association Hamburg, Germany (reference numbers PV4220 and PV4801).

Patient and public involvement

Patients or the public were not involved in the design, the reporting, or the dissemination plans of this pilot study due to its explorative nature. Patients were involved in the conduct of the trial by participating in one of the study arms. The intervention group was asked to share their experiences including burden and time expenditure associated with the intervention.

Participants

All potentially eligible patients from the outpatient clinic cohort were contacted. Inclusion criteria included diagnosis of CPPS according to the EAU guidelines [1] and the International Association for the Study of Pain [25], informed consent, age ≥ 18 years, and sufficient German

language skills. Exclusion criteria were delusional disorders or substance dependences with the exception of nicotine or painkillers, and acute suicidal tendencies. In addition, patients were not eligible for the intervention group if they had expected absences during the treatment period for more than four therapy units or received ongoing physiotherapeutic or psychotherapeutic treatment; however, participation in the control group was possible. All participants who fulfilled inclusion criteria and signed informed consent were non-randomly allocated to either intervention- or control-group. The assignment to the intervention group was based on whether the participant would be able to regularly attend the treatment sessions. The targeted overall size for the intervention group was n = 36 and n = 18 for the control group.

Intervention group

A combination of consecutive cognitive behavioural therapy (CBT) and physiotherapy was used in the intervention group. Both therapy modalities were applied in sex homogenous groups in separate modules with a four-week break between each module. The physiotherapy module was a combination of three 90-minutes group sessions and six individually scheduled treatment sessions, each lasting 60 minutes for nine weeks. Following the German physiotherapeutic concept of reflective respiratory physiotherapy (Reflektorische Atemtherapie®) [26], the single sessions included heat applications, manual techniques, specific therapeutic movements, and educational parts, whereas group sessions focused on active exercises, self-management strategies, and education. The psychotherapeutic intervention incorporated nine weekly 90-minutes group sessions CBT

including theory parts, group discussions, and Progressive Muscle Relaxation (PMR) [27]. Key topics for the cognitive behavioural intervention were behaviour analysis, positive self-messages, reduction of fear-avoidance-beliefs and behaviour, improvement of physical activity, development of coping strategies, management of catastrophizing cognitions, and enhancement of social support. A supplementary work book based on the work of Tripp et al. [28] was developed. Participants who had accumulated more than six sessions dropped out of the intervention group.

Control group

The control group received treatment as usual. Hence, they did not receive any specific treatment within this study.

Assessments

Measurements of all participants were taken at the time of the visit of the outpatient clinic (t1), during the recruitment process at baseline (t2), and at the end of the second intervention module (t6). The intervention group was assessed additionally at the beginning (t3) and the end of the first intervention module (t4), at the beginning of the second module (t5), and four weeks after the end of the second module (t7).

The primary psychometric outcome, the health-related quality of life, was measured with the 12-Item Short-Form Health Survey (SF-12) [29]. Additionally, somatic symptom severity, anxiety severity, and depression severity were assessed with the German version [30] of the Perceived Stress Questionnaire (PSQ) [31], the Patient Health Questionnaire PHQ-15 [32], the Generalized Anxiety Disorder Scale (GAD-7) [33], and the Patient Health Questionnaire PHQ-9 [34] respectively. The German version [35] of the Chronic Prostatitis Symptom Index of the National Institute of Health (NIH-CPSI) [36] and an adapted version for women with CPPS [37] were used to measure the symptom burden. Pain in conjunction with disability, perception, and catastrophizing were measured using the German version [38] of the Pain Disability Index (PDI) [39], the German version [40] of the Pain Catastrophizing Scale (PCS) [41], and the German version [42] of the Short-Form McGill Pain Questionnaire (SF-MPQ) [43]. In the physiotherapeutic examination of the intervention group, performed at the time points t3, t5, and t7, tender and trigger points in predefined muscles were manually palpated.

Statistical Analysis

Chi-square tests respectively Fisher's exact tests and t-tests for independent groups were calculated for baseline comparisons. Regarding feasibility and acceptability, the eligibility rate, the willingness-to-participate rate, and the dropout rate were calculated. Additionally, the most frequent reasons for not being eligible, not willing to participate, and for dropping-out were presented. Moreover, we compared whether absence differed between modules and whether the overall treatment satisfaction differed from each module by conducting repeated measure analyses of variance (ANOVA).

Prior to the efficacy estimations analysis, missing values in the self-report instruments were imputed using the expectation-maximization (EM) estimation method [44], provided that completion rate of a questionnaire for a particular participant at a particular time point was at least 60%. To establish consistency of efficacy estimations, all analyses were adjusted for baseline and sex as well as the interaction between sex and group affiliation at t2 and t6. The primary efficacy estimations were defined as the differences between intervention and control group after the treatment (t6) using analyses of covariance (ANCOVA) with adjustments for the respective baseline values at t2. Furthermore, potential sequence effects within the intervention group were analysed by comparing the outcomes at the end of the treatment (t6). In addition, sex effects were interpreted comparing the intervention and the control group at the end of the treatment.

Due to the exploratory nature of this study, corrections for multiple testing were not applied. For all efficacy estimations as well as comparisons of the absence and the treatment satisfaction rates, Cohen's d was calculated as an indicator of effect size. The effect sizes were classified as small ($d \geq 0.2$), medium ($d \geq 0.5$), or large ($d \geq 0.8$) [45]. Two-tailed p-values <0.05 were considered significant. All statistical analyses were conducted with IBM SPSS 24. In addition to the quantitative analyses, the trajectories for measurements of quality of life and CPPS symptoms were presented in line graphs. Furthermore, anecdotal quotes from the free text fields in the questionnaires in German were translated and used to illustrate the range of feedback.

Results

From October 2012 to June 2017, 311 persons visited the specialized outpatient clinic. Of these, 103 patients did not meet the inclusion criteria or displayed no interest in study participation at the initial screening; thus, 208 patients were further assessed for eligibility. Of these, an additional 148 patients were excluded due to failure to meet the inclusion criteria or other reasons, with 36 participants remaining in the intervention group and 24 participants remaining in the control group (Figure 1). Table 1 illustrates the demographic and psychometric characteristics of the participants. No significant differences between the groups were found.

Feasibility and satisfaction

The eligibility rate, when considering all screened persons (n = 311), was 44.7%. The main reasons for ineligibility was absence of a CPPS diagnosis and unattainability of patients. Of all eligible persons (n = 172), sixty consented to take part in the study; resulting in a willingness-to-participate rate of 34.8%. Patients who were eligible but rejected participation indicated mostly to have no interest or no time. Of the 36 persons in the intervention group, one participant dropped out prior to the first therapy unit and nine participants dropped out during the intervention period -resulting in a dropout rate of 27.8%. The adjusted average proportion of missed sessions was M = 36.33 % (SE = 4.93) for the psychotherapeutic

module, and M = 30.03 % (SE = 6.24) for the physiotherapeutic module revealing no significant differences.

In general, patients gave high ratings of treatment satisfaction (Table 2). The following quotes from the satisfaction questionnaires were selected to illustrate the breadth of patient feedback:

> *"The CPPS study has helped me managing the daily life with my pain and […] I can get better through the day. Talking about perception of the pain and its treatment […] has positively affected me."*

> *"The manual, the group, and the conversations were helpful. But I still had the need to talk and in the group, I was not confident enough to talk about everything (I would have liked to.)."*

> *"The interaction with other affected people (patients) was helpful. The contents are easy/good to take into practice. The duration of the group therapy was, in my opinion, too short. The double number of appointments would be appropriate for the input."*

Estimation of efficacy

As indicated by the main efficacy estimations, no significant differences or medium effect sizes were found for our primary outcome, the SF-12, at the end of the intervention (Table 3). With respect to the secondary outcomes, the intervention group reported significantly

lower symptom burden as measured by the PDI (p = 0.02, d = -0.73), and the PHQ-9 (p = 0.04, d = -0.62). Table 4 displays the results of the analysis of sex-related effects. Neither main effects for sex nor sex*group interaction effects were significant.

Regarding the analysis of sequence effects within the intervention group, no significant differences were found in the SF-12. With respect to the secondary outcomes, the sequence psychotherapy-physiotherapy was significantly superior to the sequence physiotherapy – psychotherapy in pain reduction as measured by the NIH-CPSI pain subscale (p = 0.03, d = -1.12).

Figure 2 displays the courses of the most important outcome variables across all times of measurement. Besides the aforementioned results, the figure suggest reductions in the Physical and Mental Component Summaries of the SF-12 and increases in the PDI, the NIH-CPSI, the PHQ-9 and the PCS between t6 and follow-up in the intervention group.

Discussion and conclusions

This study explored feasibility and acceptability of a combined psycho- and physiotherapy in patients with CPPS in terms of satisfaction, recruitment process and attendance of the participants during the treatment. Although several challenges arose during recruitment, the intended sample size could be reached and participants expressed high satisfaction with the treatment. Furthermore, we received some insights on possible treatment effects in

comparison with the treatment-as-usual group. Specifically, we found significant lower symptom burden in the intervention group as measured with the PDI and the PHQ-9 but no significant changes in the SF-12. Our results showed that the combination of psycho- and physiotherapy was feasible in general; however, based on experiences in this study, some adaptations when conducting this programme in the future seem warranted.

Compared to the literature [46], the eligibility rate and the willingness-to-participate rate were lower than the median rates in other clinical trials. One of the main reasons of the low eligibility was the circumstance that patients could refer themselves to the specialized outpatient clinic. Thus, many patients did not have a CPPS diagnosis or were only interested in the diagnostic algorithm but not in the treatment study. Moreover, the low eligibility rate might be attributed to the time lag between initial eligibility screening and trial inclusion. In our study, up to 3 ½ years have passed since the patient's last appointment at the outpatient clinic and the inquiry for the study. Since it was a rather long time, several factors might have affected eligibility: First, many patients were unattainable due to re-locations or other, mostly unknown, reasons. Second, given the natural course of chronic pain, nearly one third of the patients have less symptoms over time or are even symptom-free [47]. Third, patients with CPPS were likely to use other health care services in order to find pain relief [48]. Future trials should strive for a shorter time period between first contact with the patient and trial inclusion. Nevertheless, although the recruitment process faced these challenges, the intended sample size could be reached underlining the feasibility of the study. The feasibility of the physio- and psychotherapy combination treatment was also supported by the low dropout rates for the intervention in total and for psycho- and physiotherapy separately.

These rates were smaller in comparison to the literature [49, 50] and indicated high acceptance of the treatment. Finally, the feasibility is also indicated by the high level of satisfaction expressed by the participants. Satisfaction with the treatment is suggested to be a basic component for carrying out a successful psychotherapeutic and physiotherapeutic treatment [51]. However, directly comparing this study with existing studies is difficult, since, to the best of our knowledge, this is the first study to investigate combined physio- and psychotherapy in patients with CPPS.

While the eligibility rate was still within the interquartile range of examined studies by Gross et al. [46], the willingness-to-participate rate was considerably below the interquartile range. Although the majority of persons perceived research to be very important, the willingness to participate often depends on convenience and whether or not study participation interfered with the daily routine [52]. Moreover, patients are more likely take part in a study if the home-study site distance is short [53]. In our study, perceived lack of time, long distance to study site, and/or no interest were the most common reasons to refuse participation. Hence, these barriers should be targeted when designing future studies. One possible solution might be to concept at least some of the treatment sessions as online sessions. Not only do online programmes enable treatments independent of the home-study site distance, but also allow participants to better integrate the content of the therapy into their daily routine [54]. Furthermore, online programmes provide continuity of care during pandemic situations like the COVID-19 outbreak [55].

Besides feasibility testing, we also looked at effect sizes. Several psychometric indicators showed that the intervention group improved in comparison to the control group although only the estimation of effect size measured with the PDI and the PHQ-9 reached significance level. Nevertheless, the intervention seems to be more effective than treatment as usual in terms of reduction of pain disabilities and depressive symptoms. Interestingly, the sequence psychotherapy first, physiotherapy second appears to be more effective than the other way around. Similar findings were observed in patients with chronic neck pain, who had greater effects in pain and disability reduction as well as quality of life when combining psychotherapy with subsequent physiotherapy. The authors conclude, that patients would need the physical performance in which they can apply and train the theoretical content of the cognitive behavioural therapy [56]. We have found that the intervention effects did not differ by gender. One possible explanation could be that women and men with CPPS have similar symptom patterns. Previous studies have shown that both sexes had similar pain intensity levels [57] and that the proportion of mental disorders is elevated in comparison to the general population in both women and men [16]. Hence, with the assumption of symptoms akin, the intervention might have had worked similar for female and male patients with CPPS. Nevertheless, the sex-disaggregated subsamples were small, which might affect the effect sizes [58]. Future studies should emphasize possible sex differences in order to tailor the interventions more specifically and effectively to the respective target group.

Limitations

Some limitations of the study should be mentioned. The SF-12, the primary outcome measure, showed only a small and non-significant effect. The failure to detect a significant effect might be attributed to the small sample size of the study, but it could also be due to the generic nature of the instrument, which is not precise enough to detect changes in quality of life in patients with CPPS. This phenomenon was observed in patients with chronic low back pain [59] and thus might also be true for patients with CPPS. Usage of a CPPS-specific instrument like the NIH-CPSI [36] might be considered in future trials. Furthermore, this study is a feasibility study, which included a small, non-sufficient sample for efficacy testing. Due to the small sample, we rather focused on the effect size Cohen's d than on the statistical significance. Although the effect size is more robust in small samples than the p-value, it is not completely unaffected by sample size [58]. Owing to the construction of the study as a monocentric pilot study, allocation to intervention and control group was non-randomized, which might cause variations in the distribution of sample characteristics. However, no significant differences in study characteristics could be detected between the two branches, which does not give support for the presence of bias. Thus, at this stage of research a non-randomized feasibility study seemed reasonable. It provides first hints that a combined physio- and psychotherapy treatment might be beneficial. However, some studies, which administered either physio- or psychotherapy, exist. The German concept reflective respiratory physiotherapy as such has not been tested, but the American Wise-Anderson-Protocol includes similar therapeutic elements. A case series with male patients demonstrated decreased pain intensity and improved quality of life [60]. The psychotherapeutic programme applied in this study was tested with a group of Canadian men showing positive effects in terms of pain intensity, catastrophizing and quality of life [61]. In comparison, the combination of both therapeutic approaches in this study also indicate,

amongst other positive effects, that pain and catastrophizing decreased, and quality of life increased. Nonetheless, since existing studies are highly heterogeneous, comparing this study with available literature should be viewed with caution.

Finally, we would like to state that this study provides valuable insights for further randomized, multicentre studies; not only regarding the acceptance and the effect of the intervention, but also regarding the recruitment process. The first results of a combined physio- and psychotherapeutic treatment for patients with CPPS appear to be promising although some adaptations to the treatment programme had to be made as outlined above. Further testing of this procedure is therefore urgently needed to provide adequate and scientifically based treatment for patients with CPPS.

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Competing Interests

Gesche Ketels declares that she is a co-founder of the Association for Reflective Respiratory Physiotherapy (Verein für Reflektorische Atemtherapie e.V.), which was established in 2000. She has been a freelance lecturer for reflective respiratory physiotherapy for over 15 years. The other authors declare that they have no competing interests.

Author Contributions

Christian. A. Brünahl: Conceptualization, Writing – Review & Editing, Supervision, Project administration, Funding acquisition; ***Susanne G.R. Klotz:*** Investigation, Data Curation, Writing – Original Draft, Visualization; ***Christoph Dybowski:*** Formal analysis, Investigation, Data Curation, Writing – Review & Editing, Visualization; ***Rebecca Albrecht:*** Investigation, Writing – Review & Editing; ***Johanna Höink:*** Resources, Writing – Review & Editing; ***Margit Fisch:*** Resources, Writing – Review & Editing; ***Gesche Ketels:*** Conceptualization, Writing –

Review & Editing, Funding acquisition; ***Bernd Löwe:*** Conceptualization, Resources, Writing – Review & Editing, Supervision, Funding acquisition.

Data Sharing Statement

Technical appendix, statistical code, and dataset available upon reasonable request from the corresponding author.

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Table 1: Comparison of demographic and clinical characteristics at baseline

Variable	Intervention group (n = 36)	Control group (n = 24)	p-value
Demographic characteristics			
Female, % (n)	52.8 (19)	58.3 (14)	.67*
Age in years, mean (SD)	48.6 (±14.8)	50.6 (±14.5)	.60‡
Marital status, % (n)•	(n = 35)	(n = 22)	.29†
Single	37.1 (13)	27.3 (6)	
Married	37.1 (13)	45.5 (10)	
Divorced	25.7 (9)	18.2 (4)	
Other	0	9.1 (2)	
Educational level, % (n)•	(n = 28)	(n = 20)	.13†
6 years of secondary school	14.3 (4)	20.0 (4)	
8 years of secondary school	28.6 (8)	55.0 (11)	
High school graduation	53.6 (15)	25.0 (5)	
Other	3.6 (1)	0	
Pain duration in years, mean (SD)	6.2 (4.8)	6.2 (4.8)	.98‡
Psychometric assessments, mean (SD)			
GAD-7	7.9 (5.5)	6.5 (5.1)	.33‡
PCS	23.4 (13.6)	22.9 (16.1)	.90‡
PDI	26.7 (15.2)	26.6 (18.3)	.95‡
PHQ-9	9.9 (5.8)	9.1 (6.9)	.65‡
PHQ-15	11.0 (5.0)	10.3 (6.0)	.63‡
PSQ	0.5 (0.2)	0.5 (0.2)	.78‡
SF-12 PCS	39.5 (8.5)	38.0 (12.0)	.61‡
SF-12 MCS	39.9 (11.9)	40.2 (11.1)	.93‡
SF-MPQ total	18.2 (9.4)	18.6 (12.5)	.89‡
SF-MPQ sen.	13.2 (7.1)	14.6 (8.6)	.52‡
SF-MPQ aff.	5.0 (3.2)	4.0 (4.2)	.33‡
NIH-CPSI total	24.1 (7.4)	23.7 (7.6)	.83‡
Pain subscale	11.3 (3.8)	11.4 (3.7)	.92‡
Urinary subscale	4.7 (2.9)	4.1 (2.7)	.38‡
QoL subscale	8.0 (2.3)	8.2 (2.7)	.85‡

Legend: •assessed at outpatient clinic visit (t1); *Chi²; ‡t-test for independent samples; †Fisher's exact test; GAD-7 = Generalized Anxiety Disorder Screener; NIH-CPSI = Chronic Prostatitis Symptom Index of the National Institutes of Health; PCS = Pain Catastrophizing Scale; PDI = Pain Disability Index; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); PHQ-15 = Patient Health Questionnaire 15 (somatic symptoms); PSQ = Perceived Stress Questionnaire; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ aff. = affective subscale of Short Form McGill Pain Questionnaire; SF-MPQ sen. = sensory subscale of Short Form McGill Pain Questionnaire; SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; SD = standard deviation

Table 2: Treatment satisfaction

	All		Female		Male		Overall comparisons		
							Modules[a]	Sex	Modules*sex
	N	Est. M (SE)	N	Est. M (SE)	N	Est. M (SE)	p (d)	p (d)	p (d)
Overall treatment	25	6.0 (0.2)	14	5.9 (0.3)	11	6.2 (0.3)	0.08 (0.72)	0.37 (0.38)	0.89 (0.10)
Psychotherapeutic module	25	5.4 (0.3)	14	5.1 (0.4)	11	5.6 (0.4)			
Physiotherapeutic module	25	5.9 (0.3)	14	5.6 (0.4)	11	6.1 (0.5)			

Legend
Items: "Would you recommend …?"; scale from 1 = „does not apply at all" to 7 = "fully applies";
higher values correspond with higher treatment satisfaction.
Est. M = estimated mean; SE = standard error
[a]Overall treatment vs psychotherapeutic module vs physiotherapeutic module

Table 3: Post-treatment (t6) comparisons between the intervention group and the control group, adjusted for baseline (t2), sex, and the interaction of sex*group

	Intervention group			Control group			Comparison					
Outcome variable	n	Est. mean	SE	n	Est. mean	SE	Mean difference	ES	ES SE	ES CI 95% lower limit	ES CI 95% upper limit	p
SF-12 PCS	22	44.2	1.3	23	41.7	1.3	2.5	0.40	0.3	-0.19	0.99	0.18
SF-12 MCS	22	42.8	1.9	23	41.4	1.9	1.4	0.15	0.3	-0.43	0.74	0.61
PDI	22	18.4	2.3	22	26.5	2.4	-8.1	**-0.73**	0.3	-1.34	-0.12	**0.02**
NIH-CPSI total	22	18.6	1.5	23	20.8	1.5	-2.2	-0.31	0.3	-0.90	0.28	0.30
Pain subscale	22	8.6	0.8	23	9.5	0.8	-0.8	-0.22	0.3	-0.81	0.37	0.46
Urinary subscale	22	3.7	0.4	23	3.8	0.4	-0.1	-0.04	0.3	-0.63	0.54	0.88
QoL subscale	22	6.4	0.5	23	7.5	0.5	-1.2	-0.50	0.3	-1.10	0.09	0.10
SF-MPQ total	22	12.3	1.7	22	15.6	1.7	-3.2	-0.40	0.3	-1.00	0.20	0.19
SF-MPQ sensory	22	9.7	1.2	22	11.2	1.2	-1.5	-0.27	0.3	-0.86	0.33	0.38
SF-MPQ affective	22	2.7	0.6	22	4.2	0.6	-1.5	-0.55	0.3	-1.16	0.05	0.08
PCS	22	14.7	1.8	22	19.5	1.8	-4.8	-0.56	0.3	-1.17	0.04	0.07
PHQ-9	22	6.9	0.9	22	9.5	0.9	-2.6	**-0.62**	0.3	-1.23	-0.02	**0.04**
GAD-7	22	5.7	0.9	22	6.5	0.9	-0.9	-0.21	0.3	-0.81	0.38	0.48
PHQ-15	22	9.9	0.8	21	9.8	0.8	0.2	0.04	0.3	-0.56	0.64	0.89
PSQ	22	0.4	0.0	22	0.5	0.0	-0.0	-0.14	0.3	-0.74	0.45	0.64

Legend

p-values <.05 and corresponding ES are presented in bold

Est. = estimated; SE = standard error; ES = effect size Cohens' d; ES SE= standard error of the effect size; ES CI = confidence interval of the effect size

SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ sensory = sensory subscale of the Short Form McGill Pain Questionnaire; SF-MPQ affective = affective subscale of the Short Form McGill Pain Questionnaire; PCS = Pain Catastrophizing Scale; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); GAD-7 = Patient Health Questionnaire Generalized Anxiety Disorder Screener; PHQ-15 = Patient Health Questionnaire 15 (severity of somatic symptoms); PSQ = Perceived Stress Questionnaire

Table 4: Sex-dependent post-treatment (t6) comparisons between the intervention group and the control group

	Female patients								Male patients										
	Intervention group			Control group			Comparison		Intervention group			Control group			Comparison		Overall		
Outcome variable	n	Est. mean	SE	n	Est. mean	SE	Mean diff.	ES	n	Est. mean	SE	n	Est. mean	SE	Mean diff.	ES	ES diff.	p main effect sex	p interaction sex*group
SF-12 PCS	10	45.6	1.9	14	43.0	1.6	2.6	0.44	12	42.7	1.7	9	40.4	2.0	2.3	0.39	0.05	0.13	0.94
SF-12 MCS	10	41.0	2.9	14	39.9	2.4	1.1	0.12	12	44.6	2.6	9	42.8	3.0	1.8	0.20	-0.08	0.24	0.90
PDI	10	18.8	3.5	13	26.4	3.0	-7.6	-0.69	12	18.0	3.2	9	26.6	3.7	-8.6	-0.79	0.09	0.92	0.88
NIH-CPSI total	10	19.5	2.2	14	19.9	1.9	-0.4	-0.05	12	17.7	2.0	9	21.8	2.3	-4.1	-0.59	0.53	0.97	0.38
Pain subscale	10	8.9	1.2	14	8.9	1.0	0.0	0.01	12	8.3	1.1	9	10.0	1.2	-1.7	-0.46	0.47	0.78	0.44
Urinary subscale	10	4.3	0.7	14	3.9	0.6	0.4	0.20	12	3.0	0.6	9	3.7	0.7	-0.6	-0.29	0.50	0.23	0.41
QoL subscale	10	6.4	0.7	14	7.1	0.6	-0.8	-0.34	12	6.3	0.7	9	7.9	0.8	-1.6	-0.68	0.34	0.61	0.58
SF-MPQ total	10	12.5	2.5	13	15.6	2.2	-3.1	-0.39	12	12.2	2.3	9	15.6	2.6	-3.4	-0.43	0.04	0.93	0.94
SF-MPQ sensory	10	10.4	1.8	13	11.3	1.6	-1.0	-0.17	12	9.1	1.6	9	11.2	1.9	-2.1	-0.37	0.20	0.66	0.74
SF-MPQ affective	10	2.4	0.9	13	4.2	0.7	-1.8	-0.67	12	3.0	0.8	9	4.3	0.9	-1.3	-0.47	-0.20	0.66	0.75
PCS	10	12.6	2.7	13	19.7	2.3	-7.2	-0.86	12	16.8	2.4	9	19.2	2.8	-2.4	-0.29	-0.57	0.48	0.37
PHQ-9	10	6.9	1.3	13	10.0	1.1	-3.1	-0.75	12	6.9	1.2	9	9.0	1.4	-2.1	-0.52	-0.23	0.70	0.70
GAD-7	10	5.5	1.3	13	5.5	1.1	0.0	0.00	12	5.8	1.1	9	7.5	1.3	-1.7	-0.43	0.43	0.38	0.48
PHQ-15	10	10.3	1.1	12	9.7	1.0	0.6	0.18	12	9.5	1.0	9	9.8	1.2	-0.3	-0.09	0.27	0.74	0.67
PSQ	10	0.4	0.0	13	0.5	0.0	0.0	-0.29	12	0.5	0.0	9	0.5	0.0	0.0	0.00	-0.29	0.80	0.64

Legend:
SE = standard error; Est. = estimated; diff. = difference; ES = effect size Cohen's d
SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ sensory = sensory subscale of the Short Form McGill Pain Questionnaire; SF-MPQ affective = affective subscale of the Short Form McGill Pain Questionnaire; PCS = Pain Catastrophizing Scale; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); GAD-7 = Patient Health Questionnaire Generalized Anxiety Disorder Screener; PHQ-15 = Patient Health Questionnaire 15 (severity of somatic symptoms); PSQ = Perceived Stress Questionnaire

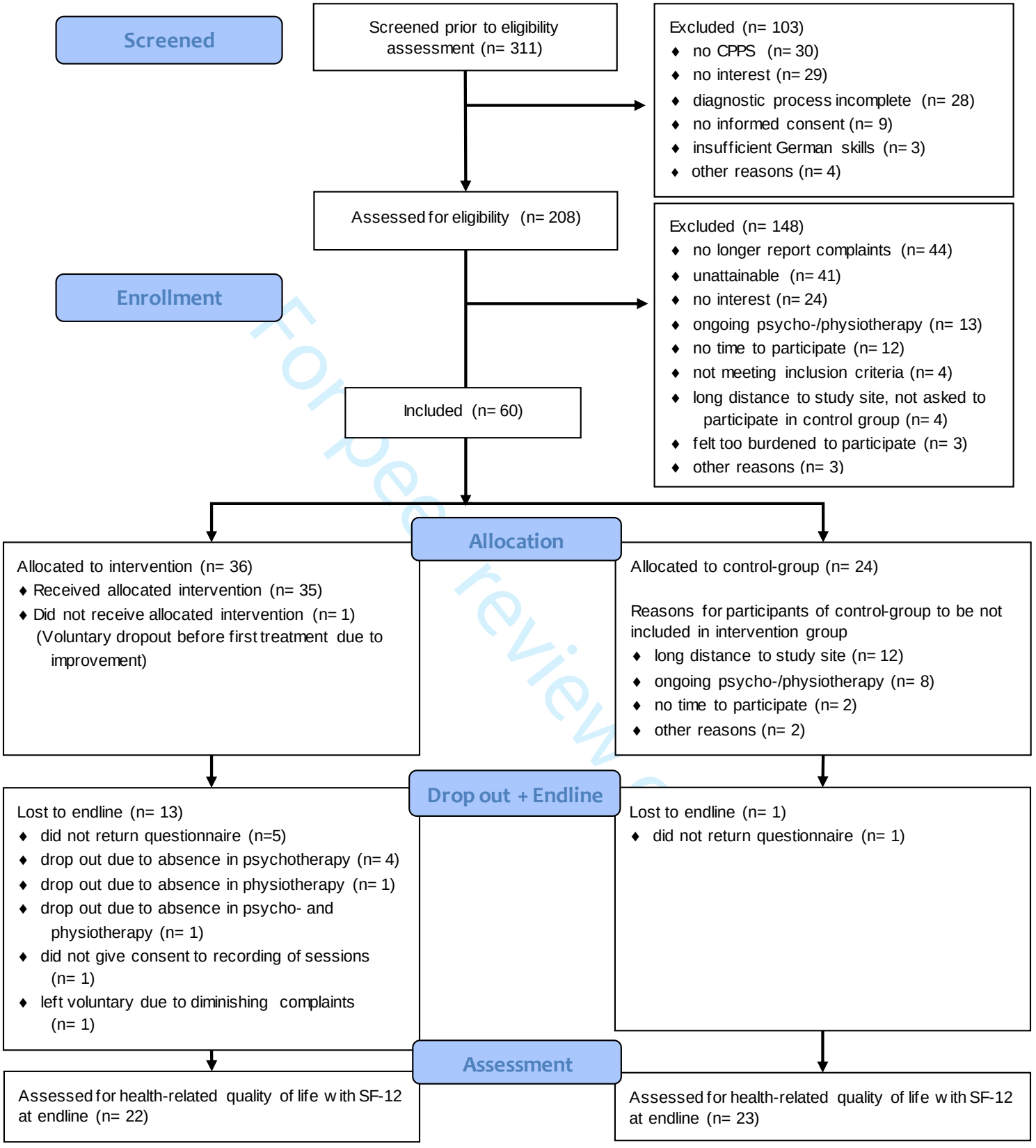
Figure 1: Flow of participants

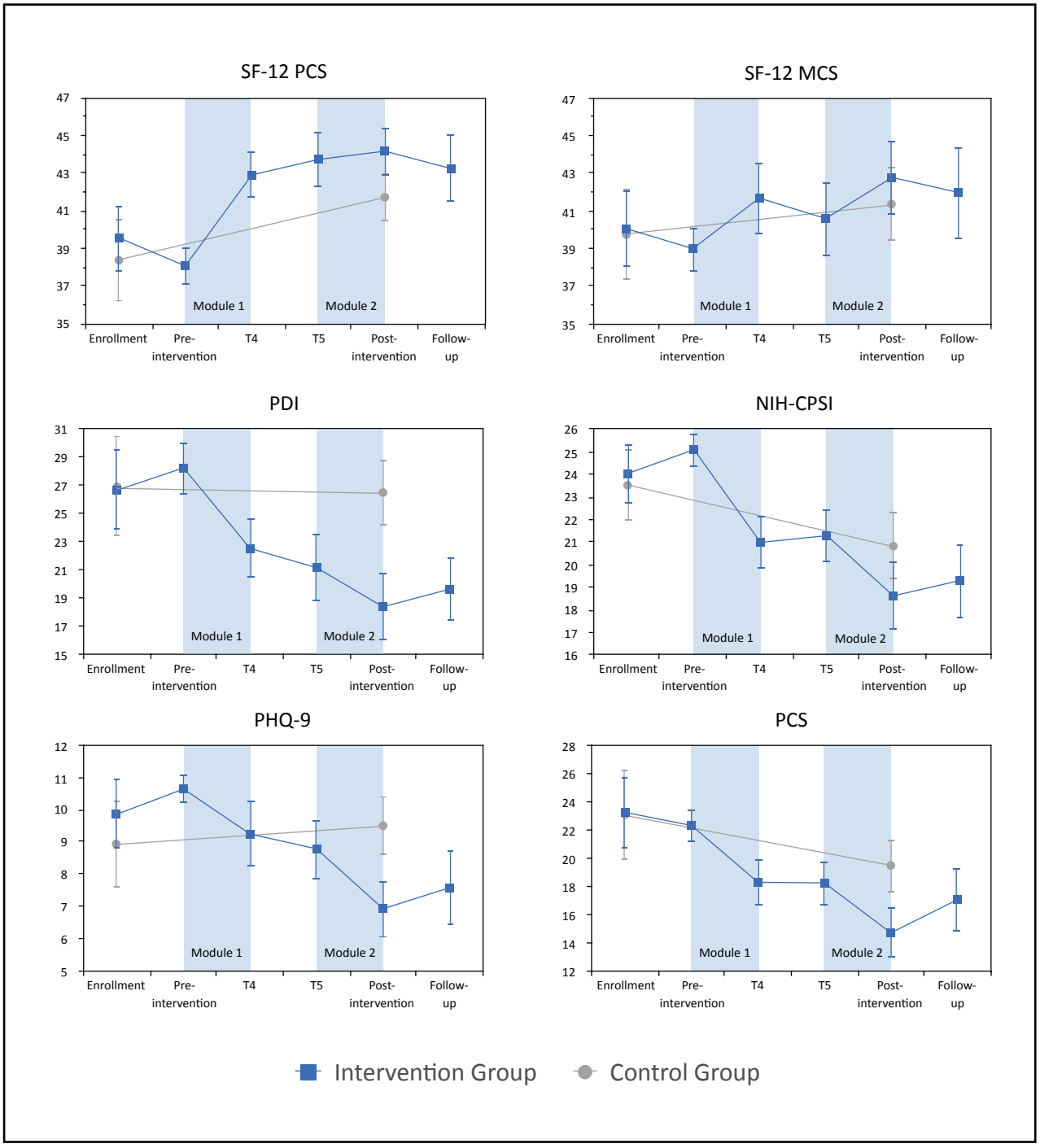
Legend: SF-12: 12-Item Short Form Health Survey

Source: Eldridge et al. (2016)

Figure 2: Course of important outcome variables in the intervention and the control group

Legend: SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; PHQ-9 = Patient Health Questionnaire 9; PCS = Pain Catastrophizing Scale




SF-12 PCS
SF-12 MCS
PDI
NIH-CPSI
PHQ-9
PCS
Module 1
Module 2
Enrollment
Pre-intervention
T4
T5
Post-intervention
Follow-up
Intervention Group
Control Group

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility trial in the title	1
	1b	Summary of pilot trial design, methods, results, and conclusions	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for pilot trial	5-6
	2b	Specific objectives or research questions for pilot trial	5-6
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	6-7
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	7-8
	4b	Settings and locations where the data were collected	6-7
	4c	How participants were identified and consented	7-8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8-9
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	9-10
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	N/A
Sample size	7a	Rationale for numbers in the pilot trial	N/A
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	N/A
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	N/A
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	N/A
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to	N/A

		interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	Figure 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	12
	14b	Why the pilot trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	Figure 1
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	12-14 Tables 2-4
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	15-19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	16-17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	15-17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	18-19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	7
Protocol	24	Where the pilot trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	20
	26	Ethical approval or approval by research review committee, confirmed with reference number	7

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.

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Trials

STUDY PROTOCOL Open Access

Combined Cognitive-Behavioural and Physiotherapeutic Therapy for Patients with Chronic Pelvic Pain Syndrome (COMBI-CPPS): study protocol for a controlled feasibility trial

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Abstract

Background: Chronic pelvic pain syndrome (CPPS) is a pain condition perceived in the pelvic area for at least 6 months. While evidence of the aetiology and maintenance of CPPS is still unclear and therapy options are rare, there is preliminary evidence for the efficacy of cognitive behavioural therapy and physiotherapy. However, an integrated treatment has not yet been studied. The primary aim of this study is therefore to test the feasibility of combined psychotherapy and physiotherapy for female and male patients with CPPS. The secondary aim is to explore changes in patient-relevant and economic outcomes compared to a control group.

Methods: A feasibility study with a crossover design based on the principles of a 'cohort multiple randomized controlled trial' will be conducted to test a combined therapy for patients with CPPS. The study will consist of two consecutive treatment modules (cognitive behavioural group psychotherapy and physiotherapy as individual and group sessions), which will be applied in varying order. The modules will consist of nine weekly sessions with a 4-week break between the modules. The control group will undergo treatment as usual. Study subjects will be recruited from the interdisciplinary outpatient clinic for CPPS at the University Medical Center Hamburg-Eppendorf. Thirty-six patients will be assigned to the intervention, and 18 patients will be assigned to the control group. The treatment groups will be gender homogeneous. Feasibility as the primary outcome will be analysed in terms of the demand, acceptability, and practicality. Secondary study outcomes will be measured using validated self-rating-scales and physical examinations.

Discussion: To the best of our knowledge, this study is the first to investigate the feasibility of combined psychotherapy and physiotherapy for patients with CPPS. In addition to testing feasibility, the results can be used for the preliminary estimation of therapeutic effects. The results from this study will be used to generate an enhanced therapeutic approach, which might be subject to further testing in a larger study.
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Background

Chronic pelvic pain syndrome (CPPS) can be described as an intermittent or constant pain condition in the pelvic area that has persisted for at least 6 months without an obvious pathology that accounts for the pain [1]. It is associated with physical symptoms suggestive of gastroenterological, urogenital, and/or sexual dysfunction [1–3] as well as with psychopathological symptoms and a reduced health-related quality of life [1, 4–15]. Psychological correlates are also emphasized by clinical phenotyping systems, such as UPOINT [16]. Thirty-four to 37% of the patients with CPPS have positive findings in the UPOINT domain 'psychosocial dysfunction'. Furthermore, 53–64% of the patients have findings in the 'tenderness of muscles' domain [17, 18], suggesting that psychotherapy and physiotherapy might be important in the treatment of patients with CPPS.

CPPS is a common pain condition with international general population prevalence rates ranging between 4 and 25% in women [8, 19–21] and between 2 and 18% in men [22–24].

Although CPPS is common, the aetiology and maintenance of CPPS are still largely unknown [25–29] and the successful management of this pain syndrome remains challenging [30, 31]. Several single-track medical and non-medical treatment strategies have failed to be sufficient [31, 32]. Therefore, a multidisciplinary approach combining medical, psychotherapeutic, and physiotherapeutic treatment strategies is recommended [1, 18, 33]. However, some psychotherapeutic and physiotherapeutic treatment strategies have shown promising effects. Cognitive behavioural therapy (CBT) strategies seem to reduce pain and symptom severity as well as increase the quality of life [34–36]. Myofascial physiotherapy techniques alone or in combination with breathing and relaxation techniques appear to be effective for treating urinary and sexual symptoms, pain, and quality of life [37–41].

Objectives

Regarding the advocacy for multimodal therapy established in the guidelines of the European Association of Urology (EAU) [1], there is an urgent need to examine combined interventions for patients with CPPS. However, due to constraints of resources, not all interventions can be tested for efficacy and effectiveness. In this case, a feasibility study can be used to decide whether a treatment method is worth further investigation and whether changes should be applied to the intervention [42].

Therefore, the primary aim of this study is to explore the feasibility of a combined psychotherapeutic and physiotherapeutic treatment for both female and male patients with CPPS. The results from this study will be used to generate an enhanced therapeutic approach, which might be subject to further testing. Additionally, the secondary objective of this study is to determine the preliminary indicators for the efficacy of this treatment programme regarding urological symptoms, psychological and physical correlates, health-related quality of life, and healthcare utilization. The results can be used to calculate the optimal sample size for a randomized controlled trial (RCT).

Methods/design

Study design

This study will be conducted based on the principles of a 'cohort multiple randomized controlled trial' (cmRCT) proposed by Relton et al. [43]. In this pragmatic study design, an observational cohort of subjects with the parameter of interest will be recruited and evaluated on a regular basis. For a randomized controlled trial, random subjects from all eligible subjects in the cohort are allocated to the intervention group, while allocation to the control group is not randomized [43].

The feasibility study is embedded in the Interdisciplinary Research Platform Chronic Pelvic Pain Syndrome (CPPS), which was initiated in 2012 at the University Medical Center Hamburg-Eppendorf to obtain insight into the somatic and psychological aspects in CPPS and to develop treatment strategies for these patients. In cooperation with different medical specialties (e.g. psychosomatic medicine, urology, gynaecology, and physiotherapy), a specialized outpatient clinic for patients with CPPS was implemented [5]. The assessment at this outpatient clinic includes a diagnosis of CPPS according to the EAU guidelines [1]. People diagnosed with CPPS constitute the observational cohort, from which subjects for this study will be recruited.

The treatment will consist of a combination of cognitive behavioural psychotherapy and physiotherapy based on an aetiological model developed especially for patients with

CPPS [6]. Psychotherapeutic and physiotherapeutic treatment modalities will be applied as consecutive modules, and both sequences will be tested (psychotherapy followed by physiotherapy vs physiotherapy followed by psychotherapy). The intervention will therefore consist of two branches, one starting with psychotherapy and the other starting with physiotherapy. For a detailed overview of the study design, see Fig. 1.

Sample

Study subjects will be recruited from the observational cohort consisting of all patients assessed at the interdisciplinary outpatient clinic for CPPS at the University Medical Center Hamburg-Eppendorf.

The following criteria will be applied to identify eligible patients in the observational cohort: CPPS diagnosis according to the EAU guidelines [1] and classification of the International Association for the Study of Pain [44], informed consent, sufficient German language skills, age > 18 years, and score ≤ 40 for the mental or physical scale of the 12-Item Short-Form Health Survey (SF-12) [45]. Exclusion criteria are delusional disorders, substance dependence (except nicotine or pain medication), acute suicidal tendencies, planned absences over the treatment period, and current psychotherapy or physiotherapy.

The targeted sample size for the study is 54 participants. Thirty-six participants will be assigned to the intervention group and 18 to the control group. This sample size allows for evaluation of the study in terms of feasibility and can be used to estimate therapeutic effects (pre–post and between groups). Although the sample size is not sufficient to prove the efficacy of the combined treatment programme, the results of the study can be used to calculate the sample size for a subsequent RCT.

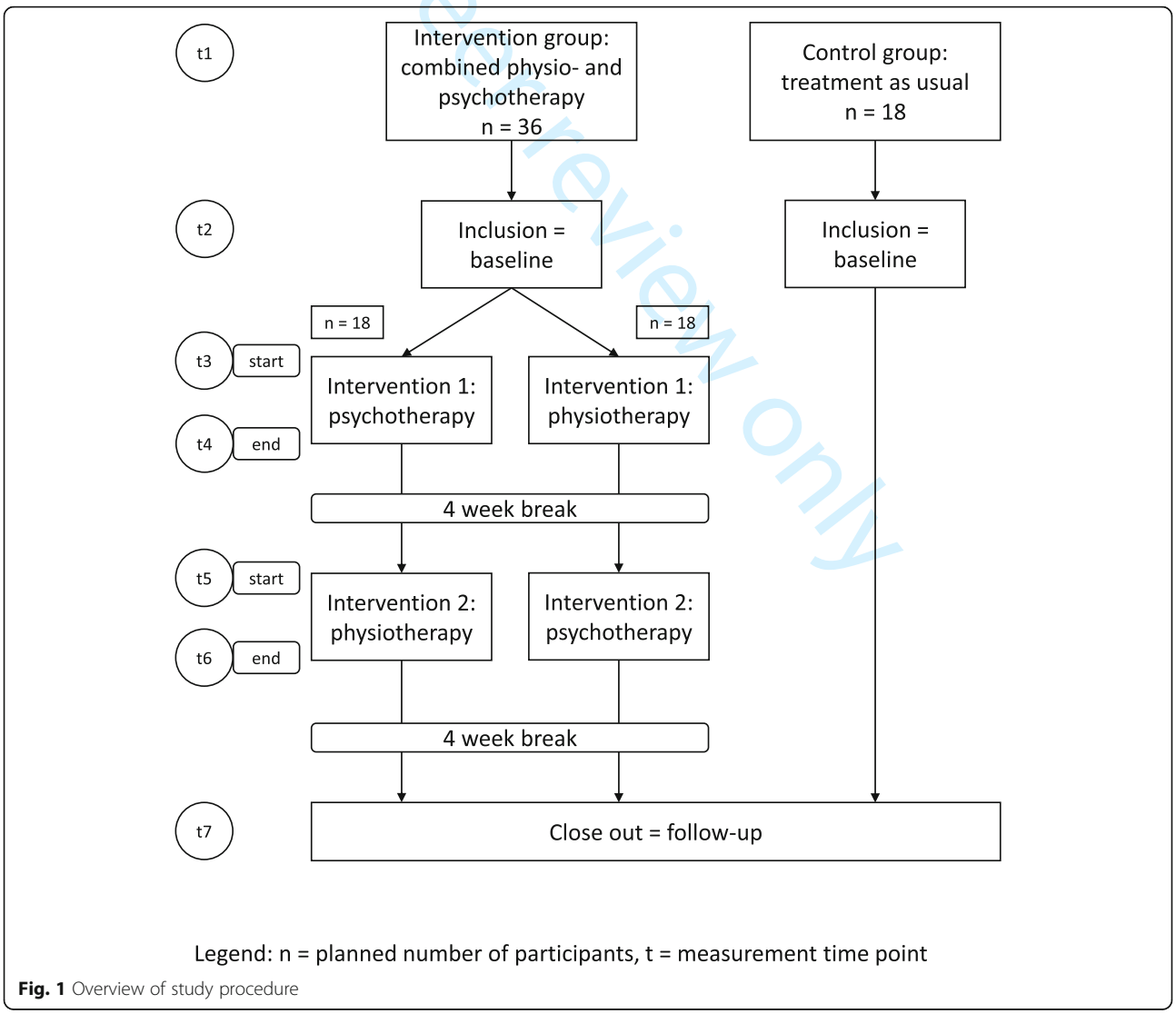

Fig. 1 Overview of study procedure

Assignment of eligible subjects to treatment and control groups will not be randomized; instead, it will be determined by the ability to regularly participate in the treatment sessions at the University Medical Center Hamburg-Eppendorf. Regular participation is defined as a maximum miss of four of the 18 treatment sessions. The assignment to one of the two treatment sequences (starting with psychotherapy vs starting with physiotherapy) will be randomized.

Procedure

In a first step, all eligible patients who were examined in the interdisciplinary CPPS outpatient clinic since 2012 (time point t1), and are thus part of the observational cohort, will be identified and assigned to either the treatment group or the control group. Detailed information about the pilot study will be sent to these patients by postal mail, whereby the informed consent signed previously by patients for the assessment at the outpatient clinic facilitates contacting them for future research. Patients willing to participate in either the treatment group or the control group will undergo a telephone interview to re-examine eligibility in case changes have occurred since their visit to the outpatient clinic and to answer open questions about the study. After inclusion, participants will receive two copies of the informed consent document, the final time schedule and a set of questionnaires (time point t2; see Instruments for a detailed description). Participants of the treatment group will also be contacted by a physiotherapist to schedule an examination appointment. Patients who do not meet inclusion criteria will be informed by telephone and will receive support regarding alternative treatment options, if requested. Patients' reasons for non-participation, if given, will be documented. In addition, patients who do not respond to the initial letter will also be contacted by telephone.

Further measurements will be conducted at the beginning (t3) and end of the first intervention module (t4) and at the beginning (t5) and the end of the second intervention module (t6) as well as 4 weeks after finishing the second intervention module (t7). The study procedure is in line with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement 2013 [46] (see also Additional file 1: SPIRIT checklist). Figure 2 displays the schedule of enrolment, interventions, and assessments according to the SPIRIT statement.

Intervention group

The intervention will consist of two consecutive treatment modules (cognitive behavioural group psychotherapy and physiotherapy as both group and individual sessions). A 4-week break is scheduled between the two modules. The intervention group has two branches; therefore, subjects will start with either one of the modules described in the following. A group size of nine patients for the psychotherapy as well as for the physiotherapy group sessions is regarded as adequate even in the event of drop-outs. This group size also reflects the maximal number of patients allowed in a CBT group in the German healthcare system [47]. The groups will be gender homogeneous because CPPS is characterized by symptoms in an intimate body region potentially associated with shame [48]. With a targeted sample size of 36 participants in the intervention and a group size of nine in the therapeutic sessions, the overall intervention group will consist of four therapeutic groups, two with only male participants and two with only female participants. One group of each gender will start with either psychotherapy or physiotherapy, resulting in four treatment groups in the intervention group.

Cognitive behavioural psychotherapy

The psychotherapeutic intervention will consist of nine weekly group sessions, each lasting 90 minutes. The sessions will be based on the following pattern: group discussion of assignments (behaviour analysis, reading a particular chapter from the patient workbook described in the following), progressive muscle relaxation (PMR) according to Jacobson [49], session-specific theory, consolidation of the specific theory through group work, concluding round, and new assignments. For a detailed overview of the CBT, see Table 1. Each session will be held by a trained and skilled CBT therapist (licensed psychotherapist) and a co-therapist (resident physician); one will be male and the other female. In order to increase generalizability we have a pool of five therapists (three female, two male) who can deliver the study intervention. All therapists will receive in-house training especially for the study and will be supervised by one specialist in CBT. During the initial session, patients will receive a printed version of the patient workbook containing theoretical background information, assignments, and repeated questionnaires regarding their symptoms for the self-evaluation of their course.

The patient workbook for cognitive behavioural group psychotherapy has been designed by members of our study group, and is based on the work of Tripp, Nickel, and Mullins [50, 51] who developed a treatment rationale for individual therapy and demonstrated its feasibility and yielded first indicators of its efficacy [35]. Through cooperation with the Canadian workgroup, we were able to translate, expand, and adapt their patient workbook [51] to the needs of our study and the German healthcare system. Key topics for the cognitive behavioural intervention are as follows:

		STUDY PERIOD					
	Outpatient clinic	Enrolment	Post-allocation				Close-out
			Start intervention 1	End intervention 1	Start intervention 2	End intervention 2	4-week follow-up
TIMEPOINT	t_1	t_2	t_3	t_4	t_5	t_6	t_7
ENROLMENT:							
Eligibility screen		X					
Informed consent		X					
Allocation		X					
INTERVENTIONS:							
Psychotherapy + Physiotherapy			←	→	←	→	
Physiotherapy + Psychotherapy			←	→	←	→	
Control group							
ASSESSMENTS:							
Sociodemographic data, case history	X						
Examination by a physical therapist	X	X			X		X
Health Care Utilization Questionnaire	X	X	X	X	X	X	X
Urological symptoms (NIH-CPSI)	X	X	X	X	X	X	X
Health-related quality of life (SF-12)	X	X	X	X	X	X	X
Pain perception (SF-MPQ)	X	X	X	X	X	X	X
Impact of pain on daily activities (PDI)	X	X	X	X	X	X	X
Catastrophizing thinking (PCS)	X	X	X	X	X	X	X
Perceived stress (PSQ)	X	X	X	X	X	X	X
Depressive symptoms (PHQ-9)	X	X	X	X	X	X	X
Somatic symptom severity (PHQ-15)	X	X	X	X	X	X	X
Generalized anxiety (GAD-7)	X	X	X	X	X	X	X
Goal attainment (GAS)*				(X)		(X)	
Patient satisfaction			X	X	X	X	

Fig. 2 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) schedule of enrolment, interventions, and assessments [46]. Legend: *GAD* = Generalized Anxiety Disorder Scale; *GAS* = Goal Attainment Scaling; *NIH-CPSI* = Chronic Prostatitis Symptom Index of the National Institute of Health; *PCS* = Pain Catastrophizing Scale; *PDI* = Pain Disability Index; *PHQ* = Patient Health Questionnaire; *PSQ* = Perceived Stress Questionnaire; *SF-MPQ* = Short-Form McGill Pain Questionnaire; *SF-12* = 12-Item Short-Form Health Survey; t = time point; * = only after the physical therapy intervention module (either at t4 or at t6)

Table 1 Overview of cognitive behavioural group psychotherapy sessions

Session	Content	Modality
1	Introduction to the programme; issuing of the patient workbook; overview of key topics; introduction to PMR	Group (90 min)
2	Group discussion/debriefing of Chapter 1 of the patient workbook; exercise of PMR; behaviour analysis	Group (90 min)
3	Group discussion/debriefing of Chapter 2 of the patient workbook; exercise of PMR; theory: catastrophizing cognitions; behaviour analysis	Group (90 min)
4	Group discussion/debriefing of Chapter 3 of the patient workbook; exercise of PMR; theory: negative self-talk; behaviour analysis	Group (90 min)
5	Group discussion/debriefing of Chapter 4 of the patient workbook; exercise of PMR; theory: influence of social relationships (Part 1); modification of 'I-message'; behaviour analysis (focus: social interaction)	Group (90 min)
6	Group discussion/debriefing of Chapter 5 of the patient workbook; exercise of PMR; theory: influence of social relationships (Part 2)/asking for support; modification of listening skills; behaviour analysis	Group (90 min)
7	Group discussion/debriefing of Chapter 6 of the patient workbook; exercise of PMR; theory: coping strategies (Part 1)/role of positive self-messages; behaviour analysis	Group (90 min)
8	Group discussion/debriefing of Chapter 7 of the patient workbook; exercise of PMR; theory: coping strategies (Part 2); activity and inactivity/recognizing avoidance behaviour; behaviour analysis	Group (90 min)
9	Group discussion/debriefing of Chapter 8 of the patient workbook; exercise of PMR; assessment of changes during the programme; revision of key topics	Group (90 min)

min minutes, *PMR* progressive muscle relaxation

- coping with catastrophizing cognitions,
- reduction of avoidance behaviour/increase of physical activity,
- development of coping strategies, and
- enhancing social support.

Furthermore, behaviour analysis also plays a key role in the programme. As group therapy facilitates the acquisition of new behaviour patterns [52], behaviour changes are addressed in the group setting. To increase the possibility of implementation into the German healthcare system we adapted the workbook to a group context.

Physiotherapy

Following the structure of the psychotherapeutic intervention, the physiotherapeutic approach is also designed in nine weekly units. However, unlike the sessions in the psychotherapy, only units 1, 5, and 9 are group treatments, while the others are designed as individual appointments. The group sessions will last 90 minutes each, and the individual sessions will last 60 minutes except for the seventh unit, which will last 90 minutes and include treatment as well as feedback and reflection about the achievement of patients' goals. Because of the more intense activity during the individual treatment and framework of ambulatory physiotherapy in the German healthcare system [53], a shorter duration was chosen in the single sessions.

The treatment is based on the Wise–Anderson Protocol, an American physiotherapeutic intervention for patients with CPPS combining trigger point therapy, a specific breathing technique, relaxation, and self-management [41, 54]. A German concept that acknowledges most of the elements of the American Wise–Anderson Protocol is Reflektorische Atemtherapie® [55, 56]. The German name of the concept is a registered trademark, and the English translation 'reflective respiratory physiotherapy' is from Zalpour [57]. This therapy aims to regulate psycho-physical coherences using the respiratory system. Specific stimuli of the connective tissue, muscles and tendons, joints, and periosteum are intended to influence the involuntary breathing and diaphragm activity. Hence, the aim is not only to improve the regulation of muscle tone and mobility, but also to affect the internal organs and pelvic floor through enhanced diaphragm mobility [58]. Positive effects of reflective respiratory physiotherapy were found in a study with patients who had chronic obstructive pulmonary disease [59].

The programme will contain the following elements [58, 60]:

- Education about the anatomy and function of the musculoskeletal system and posture with an emphasis on the pelvic floor and diaphragm, the influence of stress on the muscle tone and stiffness of fasciae, and the importance of self-management and adherence to a home exercise programme.
- Application of heat in the form of 'hot towels' (hot water-soaked towels) at the beginning of the therapy to relax muscles and joints, stimulate the circulation, and prepare the tissue for the following techniques.
- Manual techniques for all structures of the musculoskeletal system to mobilize joints and release fasciae with stretching and relaxing muscles.
- Specific therapeutic movements with partially uncomfortable or painful stimuli that influence the respiratory system and the diaphragm reflectively,

affecting the vegetative nervous system and muscle tone.
- Instruction of the patient to self-management and home exercises based on yoga to strengthen and stretch muscles, improve posture and body perception, and sense breathing activity.

In the individual sessions, subjects will be treated according to their individual findings with 'hot towels', manual techniques, and specific therapeutic movements. In addition, home exercises will be taught. During the group sessions, the focus will be on home exercises and self-management together with education and information. Similar to the psychotherapeutic group sessions, the physiotherapy group sessions will be hosted by two physiotherapists, one male and one female. Table 2 presents a scheme for the procedure and content of the physiotherapeutic intervention.

Control group

Allocation to the control group will not be randomized; instead, this will be determined by the ability to participate in the intervention occurring at the University Medical Center Hamburg-Eppendorf. It was considered difficult for patients outside the greater Hamburg area to participate; therefore, they will be allocated to the control group. The control group will not receive any specific intervention as part of the study; nonetheless, patients can seek treatment as usual from their local healthcare provider. Assessment of the control group will be done at two time points; first, at time point t2, which is the enrolment time; and second, at time point t7, which is 4 weeks after the intervention group has finished the second intervention module. The results of these measurements will be compared with the results of the intervention group to gather initial insight into the efficacy of the intervention compared to treatment as usual.

Instruments

The assessment at our interdisciplinary CPPS outpatient clinic constitutes the measurement time point t1. This involves collection of socio-demographic data and the case history, an examination by a physiotherapist, and completion of psychometric questionnaires used in this study. For an overview of the instruments used in this study, see Fig. 2.

Feasibility will be operationalized using information from the participants, therapists, and those involved in organization of the study. Information from participants will include the response rate to study invitation, willingness to participate, and reasons for not participating as indicators of demand. Practicality will be operationalized in terms of the time and personnel expenditures. Attendance at and satisfaction with physiotherapy and psychotherapy sessions, the number of drop-outs and adverse events, and the amount of missing data in the questionnaires of the workbook will function as indicators of acceptability. To assess satisfaction, we developed questionnaires using 7-point Likert scales. Subjects will be asked to rate each psychotherapeutic and physiotherapeutic session, including the accompanying study materials, each whole treatment module (psychotherapy or physiotherapy), and overall contentment with the combination of psychotherapy and physiotherapy. The questionnaires cover therapeutic and organizational aspects.

The secondary objectives of the feasibility study will be measured using the following instruments:

Table 2 Overview of physiotherapy sessions

Session	Content	Modality
1	Relationship between muscle tension, stress, and pain; awareness of tension and relaxation of the pelvic floor muscles; instruction of home exercises/self-management; goal attainment scaling	Group (90 min)
2	Reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
3	Reflection of the past sessions; reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
4	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
5	Reflection of the past group session; instruction of home exercises/self-management	Group (90 min)
6	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
7	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
	Feedback for the individual sessions; evaluation of and reflection on goal attainment; self-management	Single (30 min)
8	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
9	Evaluation of and reflection on goal attainment; self-management; home exercises; feedback and conclusion	Group (90 min)

min minutes

- The health-related quality of life will be assessed using the SF-12 [45], which has been demonstrated as reliable and valid in clinical and population-based samples [61, 62].
- The Chronic Prostatitis Symptom Index of the National Institute of Health (NIH-CPSI) [63] is considered the criterion standard for assessing urological symptom severity in CPPS in the EAU guidelines [1]. The German version with good psychometric properties [64] will be applied in this study. Since the original NIH-CPSI was designed for male patients, a modified version for female patients also exists [65].
- The German version [66] of the Short-Form McGill Pain Questionnaire (SF-MPQ) [67] will be used to assess pain perception.
- The impact of pain on the ability to participate in essential life activities will be measured with the Pain Disability Index (PDI) [68, 69], a valid and reliable [70] instrument.
- Pain catastrophization will be assessed with the aid of the Pain Catastrophizing Scale (PCS) [71], which has been shown to have good psychometric properties [72].
- To quantify the psychological symptom burden, three subscales of the German version of the Patient Health Questionnaire (PHQ-D) [73] with good psychometric characteristics [74–76] will be applied: the PHQ-9 for measuring depressive symptoms [77], the PHQ-15 for measuring the severity of somatic symptoms [78], and the Generalized Anxiety Disorder Scale (GAD-7) [76, 79] for measuring symptoms of generalized anxiety.
- The reliable and valid [80] German short version [81] of the Perceived Stress Questionnaire (PSQ) [82] will be used to assess subjectively experienced stress.
- Assessment of tender and trigger points in the abdominal wall, bottom, thighs, and pelvic floor is done with external and internal manual palpation. Although the reliability of manual palpation is variable [83, 84], it is essential in finding painful points in the muscles [85–87]. In female subjects, internal palpation is done via the vagina and rectum; in male subjects, internal palpation is done via the rectum. Prior to this examination, patients gave written informed consent to internal palpation.
- Participants set their individual therapy goals on the participation level of the International Classification of Functioning, Disability and Health [88] in the first physiotherapeutic group session and evaluate them in the last group treatment using the reliable and valid [89–92] Goal Attainment Scaling (GAS) [93].
- To assess healthcare utilization, we are using the Health Care Utilization Questionnaire, which is a modified version of the Client Socio-Demographic and Service Receipt Inventory—European Version [94] and was developed by the Institute of Health Economics and Health Services Research of the University Medical Center Hamburg-Eppendorf.

Data management and analysis

After completion of data collection, raw data will be entered in prepared electronic databases and merged with the electronically captured data. The accuracy of data will be checked by two independent researchers. Data saving and storage will be performed in accordance with the German regulation of Good Clinical Practice [95].

In addition to the quantitative data, feasibility will be analysed using qualitative data, such as answers to open questions in the satisfaction questionnaires and verbal information.

Descriptive statistics will be used to summarize the sample characteristics (e.g. sex, age, and symptom duration) and two-tailed independent *t*-tests will be used to test for significant differences between the intervention and control groups at enrolment (t2).

Subjects will be analysed on an intention-to-treat basis. To examine the course of the symptoms, related variables will be analysed using the pre–post point estimate comparisons, variability estimates, and 95% confidence intervals. The controlled study design allows for within-group as well as between-group comparisons. Paired-sample *t*-tests will be used for within-group comparisons, while the independent *t*-test will be used for between-group comparisons.

The significance level for all *t*-tests will be set at $p < 0.05$.

The analyses of the course of the symptom-related variables will function as estimates of the effect sizes, while effect estimates can be obtained for physiotherapy and psychotherapy separately as well as the overall effect estimates. These estimates can be used to determine the optimal sample size for a subsequent RCT with a normally distributed sample; hence, parametric tests will be applied as statistical procedures in the feasibility study. Factors influencing therapy success will also be examined.

Statistical analyses will be performed with IBM SPSS Statistics, Version 24 (IBM, Armonk, NY, USA).

Discussion

This article describes the research protocol for a controlled feasibility study of a combination of psychotherapeutic and physiotherapeutic treatments for patients with CPPS. The study will use an interdisciplinary short-term group intervention consisting of psychotherapy and physiotherapy for testing feasibility of the

combined intervention as well as providing the first indicators of efficacy.

The group assignment will be based on the ability of regular participation in the intervention which might lead to selection bias. However, we deemed regular attendance important for the positive effect of the whole intervention programme, and as the complete intervention will last 22 weeks (each intervention module has a duration of 9 weeks with a 4-week break in between) it will require a great concession in terms of time. Participants will not only have a weekly appointment at University Medical Center Hamburg-Eppendorf, they will also have to prepare the psychotherapeutic sessions by reading the workbook chapters and completing the respective questionnaires. It is unclear whether patients will comply with these requirements so that they will be prepared enough to follow and understand the content of the single psychotherapeutic sessions. Moreover, it is expected that at least some subjects will miss one or more sessions due to shift work, unplanned vacations, or other reasons. This might result in difficulties in understanding the content of the subsequent sessions, influencing the effect of the intervention. However, the subjects will have manuals for both the psychotherapy and physiotherapy components, which will allow them to educate themselves even if they have missed a session. Both intervention modules will be applied in a subsequent order rather than to deliver physiotherapy and psychotherapy at the same time. This approach was chosen so that participants have to make time for a weekly appointment and estimate the effects of each module separately. Nonetheless, some patients might find it tempting to select the intervention module they find more interesting or suitable for their individual situation and skip the other one. In addition, the subsequent order contributes to the prolongation of the overall treatment period. All psychotherapy sessions will be provided as group treatments. Group sessions will be accompanied by a workbook, which requires that participants adhere to specific assignments and may influence their motivation. Nonetheless, the workbook provides support and advice both during the intervention period and after its completion.

Prior studies suggest that physiotherapy is highly valued by patients with CPPS [6, 96] and can empower them to take responsibility for themselves and their coping with pain [97]. During the design of the intervention, the aspect of empowerment and self-management was emphasized, which was a strength of the study. Moreover, instead of adapting a foreign concept such as the Wise–Anderson Protocol [54], a German, already implemented, physiotherapeutic management approach was used. The combination of physiotherapeutic group and individual sessions is not part of the regular health care in ambulatory settings in Germany and might be unexpected for some participants. While they will be in a confidential setting during individual treatments with the physiotherapist, they will have to cope with several other patients being present during performance of exercises. Nevertheless, this group experience can also have a positive effect on the subjects.

We intend to recruit patients from the CPPS outpatient clinic, which has been ongoing since 2012 and serves as the observational cohort in our study design. This cohort is limited in size, and it could be brought into question whether sufficient patients are willing to participate and fulfil eligibility criteria. Their initial assessment at the outpatient clinic might be several months to years prior and their situation with regard, but non-exclusive, to the CPPS might have changed, resulting in non-participation in the study. However, this feasibility study should provide information for further optimization of the treatment approach and power calculation in future RCTs rather than sufficient testing of programme effects. Because of the exploratory nature of the study, no sample calculation was performed, and the selection of controls was based on pragmatic reasons. Nevertheless, to the authors' knowledge, this study is the first to evaluate a combined programme of psychotherapy and physiotherapy for patients with CPPS while acknowledging the multifactorial aetiology and demand for multimodal therapies [1, 17].

Trial status

The study is currently ongoing. Recruitment of patients started in mid-May 2016 and will continue until the targeted sample size is reached. The first two groups, one that started with physiotherapy and the other with psychotherapy, underwent treatment from June to November 2016. The second two groups started in January 2017 and will be treated until June 2017. The next two groups are supposed to start treatment in July 2017.

Additional file

Additional file 1: Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist (DOC 120 kb)

Abbreviations

CBT: Cognitive behavioural therapy; cmRCT: Cohort multiple randomized controlled trial; CPPS: Chronic Pelvic Pain Syndrome; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders IV; EAU: European Association of Urology; GAD-7: Generalized Anxiety Disorder Scale; GAS: Goal Attainment Scaling; NIH-CPSI: Chronic Prostatitis Symptom Index of the National Institute of Health; PCS: Pain Catastrophizing Scale; PDI: Pain Disability Index; PHQ: Patient Health Questionnaire; PMR: Progressive muscle relaxation; PSQ: Perceived Stress Questionnaire; RCT: Randomized controlled trial; SCID: Structured Clinical Interview for DSM-IV Axis I Disorders; SF-12: 12-Item Short-Form Health Survey; SF-MPQ: Short-Form McGill Pain Questionnaire

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Availability of data and materials
The datasets which will be generated during the current study will be available from the corresponding author on reasonable request.

Participants' safety and adverse events
Participants will be covered by the patient insurance of the University Medical Center Hamburg-Eppendorf. Both the psychotherapy and the physiotherapy will be conducted by health professionals trained specifically and knowledgeable in safe application as well as appraisal of the therapy modalities. However, in case of any adverse event, medical care is available at any time through the University Medical Center Hamburg-Eppendorf. All adverse events will be documented and serious adverse events will be reported to the ethics committee within one working day.

Authors' contributions
CAB is responsible for study design, project management, and editing of the manuscript. SGRK is responsible for writing of the manuscript. CD is responsible for critical revision of the manuscript. BR is responsible for study design and critical revision of the manuscript. SG is responsible for writing of the manuscript. DAT is responsible for preliminary work in the design of the psychotherapeutic treatment rationale and patient workbook. GK is responsible for study design, project management, and editing of the manuscript. BL is responsible for study design, project management, supervision of the study, and editing of the manuscript. All authors commented on the draft and approved the final manuscript.

Ethics approval and consent to participate
The study protocol has been conducted according to the Declaration of Helsinki and has been approved by the Ethics Committee of the Medical Association Hamburg, Germany (2 December 2014; reference number PV4801). Patients, who were contacted during recruitment, have given their consent to be contacted in the future during the initial examination at the CPPS outpatient clinic (which has been approved by the Ethics Committee of the Medical Association Hamburg, Germany; 17 August 2012; reference number PV4220). Patients participating in the feasibility study will sign a separate informed consent form that has been approved by the ethics committee. The informed consent in duplicate will be send to the participants by mail.

Consent for publication
Not applicable.

Competing interests
GK declares that she is a co-founder of the Association for Reflective Respiratory Physiotherapy (Verein für Reflektorische Atemtherapie e.V.), which was established in 2000. She has been a freelance lecturer for reflective respiratory physiotherapy for over 15 years. The other authors declare that they have no competing interests.

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Physiotherapy and Combined Cognitive-Behavioural Therapy for Patients with Chronic Pelvic Pain Syndrome: Results of a Non-Randomized Controlled Feasibility Trial.

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Abstract

Objective: To explore feasibility in terms of delivering and evaluating a combination of physio- and psychotherapy for patients with chronic pelvic pain syndrome (CPPS).

Design: Prospective non-randomized controlled pilot study.

Setting: Tertiary care facility with a specialized interdisciplinary outpatient clinic for patients with CPPS.

Participants: A total of 311 patients was approached; 60 participated. Thirty-six patients were included in the intervention group (mean age ± SD 48.6 years ± 14.8; 52.8% female) and 24 in the control group (mean age ± SD 50.6 years ± 14.5; 58.3% female). Fourteen participants were lost to follow up.

Interventions: Participants were non-randomly allocated to the intervention group with two consecutive treatment modules (physiotherapy and cognitive behavioural therapy) with a duration of nine weeks each or to the control group (treatment as usual).

Main outcome measures: Feasibility was operationalized in terms of delivering and evaluating the therapeutic combination. Regarding eligibility as the first aspect of feasibility, willingness to participate, drop-out, and satisfaction were assessed; for the second aspect standardized self-report questionnaires measuring health-related quality of life, depression severity, and pain were applied.

Results: Although eligibility and willingness-to-participate rates were low, satisfaction of the participants in the intervention group was high and drop-out rates were low. Results indicated a small and non-significant intervention effect in health-related quality of life and significant effects regarding depression severity and pain.

Conclusions: The combination of physio- and psychotherapy for patients with CPPS seems to be feasible and potentially promising with regard to effect. However, a subsequent fully powered randomized controlled trial is needed.

Trial registration: German Clinical Trials Register (DRKS00009976) and ISRCTN (ISRCTN43221600).

Keywords: chronic pelvic pain syndrome, cognitive behavioural therapy, physiotherapy, interdisciplinary treatment, feasibility study

Article Summary

Strengths and limitations of this study

- A feasibility study was conducted to evaluate the combination of physiotherapy and psychotherapy in patients with chronic pelvic pain syndrome.
- Inclusion of both women and men acknowledging the affectedness of both sexes.
- Besides feasibility testing, several patient relevant outcomes with a focus on quality-of-life and pain-related issues were examined.
- A control group was utilised; however, allocation to the study arms was not randomized.

Introduction

Chronic pelvic pain syndrome (CPPS) is a common chronic pain condition with pain perceived in pelvis-related structures and organs without an apparent pathology for at least six months [1]. Worldwide, prevalence rates in the general population range from 4% to 26.6% in women [2, 3] and 2% to 18% in men [4, 5]. Several risk and contributing factors exist [6], but the aetiology of CPPS is still unclear [7].

Several treatment strategies including psychotherapeutic and physiotherapeutic approaches exist, yet for most of these programmes, a distinct benefit was not found [8-11]. The physiotherapeutic approach with the currently best evidence with respect to pain reduction and improvement in quality of life is manual trigger point therapy alone or in combination with active therapy elements [11]. As for psychotherapy, somatocognitive approaches which encourage body awareness and reflection on pain cognitions might be helpful in reducing pain as demonstrated in a randomized-controlled trial [10]. However, existing reviews demonstrated that the successful treatment of CPPS remains challenging and that single treatment strategies often fail to be satisfactory [9]. A combination of physio- and psychotherapy might be a promising approach in reducing symptoms and increasing quality of life [10], so that a multidisciplinary treatment approach is highly recommended [1, 8, 12]. Nonetheless, to the best of our knowledge, no study has tested the combination of physio- and psychotherapy.

Another argument for a combination of treatment modalities is the heterogeneity of symptoms among patients with CPPS. The spectrum includes urogenital, gastroenterological, and/or sexual dysfunction [13]. CPPS is also associated with myofascial [12, 14] and psychopathological symptoms as well as a decreased health-related quality of life [12, 15-20]. Furthermore, there seems to be a linkage between myofascial and psychosocial factors [14]. The aim of this study was to explore the feasibility of combining physio- and psychotherapy in a common therapy approach for female and male patients with CPPS in terms of delivering and evaluating the therapeutic combination.

Material and Methods

Study design

The study was based on the principles of a "cohort multiple randomized controlled trial" (cmRCT) proposed by Relton et al. [21] Participants were recruited from a specialized outpatient clinic for patients with CPPS based at the University Medical Centre Hamburg-Eppendorf. From August 2012 to December 2017, several studies were conducted within the *Interdisciplinary Research Platform Chronic Pelvic Pain Syndrome (CPPS)* [11, 14-20, 22-24]. In the CPPS outpatient clinic, patients underwent multimodal diagnostic algorithm consisting of psychosomatic, physiotherapeutic, urologic, and gynaecologic assessments. Patients signed informed consent, which allowed the contact for this study. The protocol for the study was

published [23] and the study was registered at the German Clinical Trials Register (DRKS00009976) and at ISRCTN (ISRCTN43221600). Ethical approval for the CPPS outpatient clinic and for the feasibility study was given by the Ethics Committee of the Medical Association Hamburg, Germany (reference numbers PV4220 and PV4801).

Patient and public involvement

Patients or the public were not involved in the design, the reporting, or the dissemination plans of this pilot study due to its explorative nature. Patients were involved in the conduct of the trial by participating in one of the study arms. The intervention group was asked to share their experiences including burden and time expenditure associated with the intervention.

Participants

All potentially eligible patients from the outpatient clinic cohort were contacted. Inclusion criteria included diagnosis of CPPS according to the EAU guidelines [1] and the International Association for the Study of Pain [25], informed consent, age ≥ 18 years, and sufficient German language skills. Exclusion criteria were delusional disorders or substance dependences with the exception of nicotine or painkillers, and acute suicidal tendencies. In addition, patients were not eligible for the intervention group if they had expected absences during the treatment period for more than four therapy units or received ongoing physiotherapeutic or

psychotherapeutic treatment; however, participation in the control group was possible. All participants who fulfilled inclusion criteria and signed informed consent were non-randomly allocated to either intervention- or control-group. The assignment to the intervention group was based on whether the participant would be able to regularly attend the treatment sessions at the University Medical Centre Hamburg-Eppendorf. The targeted overall size for the intervention group was n = 36 and n = 18 for the control group.

Intervention group

A combination of consecutive cognitive behavioural therapy (CBT) and physiotherapy was used in the intervention group. Both therapy modalities were applied in sex homogenous groups in separate modules with a four-week break between each module. The physiotherapy module was a combination of three 90-minutes group sessions and six individually scheduled treatment sessions, each lasting 60 minutes for nine weeks. Following the German physiotherapeutic concept of reflective respiratory physiotherapy (Reflektorische Atemtherapie®) [26], the single sessions included heat applications, manual techniques, specific therapeutic movements, and educational parts, whereas group sessions focused on active exercises, self-management strategies, and education. The psychotherapeutic intervention incorporated nine weekly 90-minutes group sessions CBT including theory parts, group discussions, and Progressive Muscle Relaxation (PMR) [27]. Key topics for the cognitive behavioural intervention were behaviour analysis, positive self-messages, reduction of fear-avoidance-beliefs and behaviour, improvement of physical activity, development of coping strategies, management of catastrophizing cognitions, and

enhancement of social support. A supplementary work book based on the work of Tripp et al. [28] was developed. Participants who had accumulated more than six sessions dropped out of the intervention group.

Control group

The control group received treatment as usual. The patients were allowed to participate in standard medical care as performed in Germany. This includes, for example, outpatient treatment by a general practitioner or specialist. Hence, they did not receive any specific treatment within this study.

Assessments

Measurements of all participants were taken at the time of the visit of the outpatient clinic (t1), during the recruitment process at baseline (t2), and at the end of the second intervention module (t6). The intervention group was assessed additionally at the beginning (t3) and the end of the first intervention module (t4), at the beginning of the second module (t5), and four weeks after the end of the second module (t7).

Feasibility of delivering the combined intervention was operationalized in terms of willingness-to-participate, reasons for refusing to participate and attendance rate. In addition, the acceptance of this therapeutic intervention by the patients was operationalized

by a questionnaire assessing the satisfaction of the participants. This questionnaire was designed specifically for this study and contained Likert scales as well as open questions, which gave participants the opportunity to share their thoughts on this combined intervention.

A major concern of this feasibility study was also to provide effect sizes for power calculations for randomized clinical trials to be planned in the future. For this purpose, the effect sizes for different self-report scales were calculated. A power calculation for the present study was consequently not performed, also due to the nature of a feasibility study. The conduct of the inferential statistical analyses, including the determination of effect sizes, also served to analyze the feasibility of the analysis methods for future studies. When interpreting statistical significance in the context of this study, the small sample size, the insufficient power and the non-randomized design must be taken into account. Thus, the main psychometric outcome for the feasibility of the evaluation, the health-related quality of life, was measured with the 12-Item Short-Form Health Survey (SF-12) [29]. Additionally, somatic symptom severity, anxiety severity, and depression severity were assessed with the German version [30] of the Perceived Stress Questionnaire (PSQ) [31], the Patient Health Questionnaire PHQ-15 [32], the Generalized Anxiety Disorder Scale (GAD-7) [33], and the Patient Health Questionnaire PHQ-9 [34] respectively. The German version [35] of the Chronic Prostatitis Symptom Index of the National Institute of Health (NIH-CPSI) [36] and an adapted version for women with CPPS [37] were used to measure the symptom burden. Pain in conjunction with disability, perception, and catastrophizing were measured using the German version [38] of the Pain Disability Index (PDI) [39], the German version [40] of the Pain Catastrophizing Scale (PCS) [41], and the German version [42] of the Short-Form McGill Pain Questionnaire (SF-MPQ) [43]. In the

physiotherapeutic examination of the intervention group, performed at the time points t3, t5, and t7, tender and trigger points in predefined muscles were manually palpated.

Two adaptations in the outcome measures had to be made after registration: Originally, it was planned to use attainment of individual patient goals in the intervention group measured with the goal attainment scale after each module and four weeks after overall treatment. However, the patients were not used to goal setting and the assessment of their goals resulted in feelings of discomfort and insecurity. Hence, goal attainment was dropped as an outcome. The other previously planned outcome, selective attention on pain-related stimuli as measured by a computer-based dot-probe-task, was also dropped due to technical difficulties, which arose during the study process.

Statistical Analysis

Chi-square tests respectively Fisher's exact tests and t-tests for independent groups were calculated for baseline comparisons. Regarding feasibility with emphasis on acceptance, the eligibility rate, the willingness-to-participate rate, and the dropout rate were calculated. Additionally, the most frequent reasons for not being eligible, not willing to participate, and for dropping-out were presented. Moreover, we compared whether absence differed between modules and whether the overall treatment satisfaction differed from each module by conducting repeated measure analyses of variance (ANOVA).

Prior to the efficacy estimation analysis, which was done in order to gain insight into feasibility of evaluation, missing values in the self-report instruments were imputed using the expectation-maximization (EM) estimation method [44], provided that completion rate of a questionnaire for a particular participant at a particular time point was at least 60%. To establish consistency of efficacy estimations, all analyses were adjusted for baseline and sex as well as the interaction between sex and group affiliation at t2 and t6. The primary efficacy estimations were defined as the differences between intervention and control group after the treatment (t6) using analyses of covariance (ANCOVA) with adjustments for the respective baseline values at t2. Furthermore, potential sequence effects within the intervention group (psychotherapy followed by physiotherapy vs physiotherapy followed by psychotherapy) were analysed by comparing the outcomes at the end of the treatment (t6). In addition, sex effects were interpreted comparing the intervention and the control group at the end of the treatment.

Due to the exploratory nature of this study, corrections for multiple testing were not applied. For all efficacy estimations as well as comparisons of the absence and the treatment satisfaction rates, Cohen's d was calculated as an indicator of effect size. The effect sizes were classified as small ($d \geq 0.2$), medium ($d \geq 0.5$), or large ($d \geq 0.8$) [45]. Two-tailed p-values <0.05 were considered significant. All statistical analyses were conducted with IBM SPSS 24. In addition to the quantitative analyses, the trajectories for measurements of quality of life and CPPS symptoms were presented in line graphs. Furthermore, anecdotal quotes from the free text fields in the questionnaires in German were translated and used to illustrate the range of feedback.

Results

From October 2012 to June 2017, 311 persons visited the specialized outpatient clinic. Of these, 103 patients did not meet the inclusion criteria or displayed no interest in study participation at the initial screening; thus, 208 patients were further assessed for eligibility. Of these, an additional 148 patients were excluded due to failure to meet the inclusion criteria or other reasons, with 36 participants remaining in the intervention group and 24 participants remaining in the control group (Figure 1). Table 1 illustrates the demographic and psychometric characteristics of the participants. No significant differences between the groups were found.

Feasibility of delivering and satisfaction

The eligibility rate, when considering all screened persons (n = 311), was 44.7%. The main reasons for ineligibility was absence of a CPPS diagnosis and unattainability of patients. Of all eligible persons (n = 172), sixty consented to take part in the study; resulting in a willingness-to-participate rate of 34.8%. Patients who were eligible but rejected participation indicated mostly to have no interest or no time. Of the 36 persons in the intervention group, one participant dropped out prior to the first therapy unit and nine participants dropped out during the intervention period -resulting in a dropout rate of 27.8%. The adjusted average proportion of missed sessions was M = 36.33 % (SE = 4.93) for the psychotherapeutic

module, and M = 30.03 % (SE = 6.24) for the physiotherapeutic module revealing no significant differences.

In general, patients gave high ratings of treatment satisfaction (Table 2). The following quotes from the satisfaction questionnaires were selected to illustrate the breadth of patient feedback:

> *"The CPPS study has helped me managing the daily life with my pain and […] I can get better through the day. Talking about perception of the pain and its treatment […] has positively affected me."*

> *"The manual, the group, and the conversations were helpful. But I still had the need to talk and in the group, I was not confident enough to talk about everything (I would have liked to.)."*

> *"The interaction with other affected people (patients) was helpful. The contents are easy/good to take into practice. The duration of the group therapy was, in my opinion, too short. The double number of appointments would be appropriate for the input."*

Feasibility of evaluation and estimation of efficacy

As indicated by the main efficacy estimations, which serve as indicators for feasibility of evaluation, no significant differences or medium effect sizes were found for the SF-12 at the end of the intervention (Table 3). With respect to the secondary outcomes, the intervention

group reported significantly lower symptom burden as measured by the PDI (p = 0.02, d = -0.73), and the PHQ-9 (p = 0.04, d = -0.62). Table 4 displays the results of the analysis of sex-related effects. Neither main effects for sex nor sex*group interaction effects were significant.

Regarding the analysis of sequence effects within the intervention group, no significant differences were found in the SF-12. With respect to the secondary outcomes, the sequence psychotherapy-physiotherapy was significantly superior to the sequence physiotherapy – psychotherapy in pain reduction as measured by the NIH-CPSI pain subscale (p = 0.03, d = -1.12).

Figure 2 displays the courses of the most important outcome variables across all times of measurement. Besides the aforementioned results, the figure suggests reductions in the Physical and Mental Component Summaries of the SF-12 and increases in the PDI, the NIH-CPSI, the PHQ-9 and the PCS between t6 and follow-up in the intervention group.

Discussion and conclusions

This study explored feasibility of a combined psycho- and physiotherapy in patients with CPPS in terms of delivering and evaluating. Although several challenges arose during recruitment, the intended sample size could be reached and participants expressed high satisfaction with the treatment. Furthermore, we received some insights on possible

treatment effects in comparison with the treatment-as-usual group. Specifically, we found significant lower symptom burden in the intervention group as measured with the PDI and the PHQ-9 but no significant changes in the SF-12. Our results showed that delivering a combination of psycho- and physiotherapy was feasible; however, based on experiences in this study, some adaptations when conducting this programme in the future seem necessary. The evaluation of this intervention also demonstrated to be feasible using analysis of covariances; however, some instruments seemed to be more suitable in demonstrating effects than others.

Compared to the literature [46], the eligibility rate and the willingness-to-participate rate were lower than the median rates in other clinical trials. One of the main reasons of the low eligibility was the circumstance that patients could refer themselves to the specialized outpatient clinic. Thus, many patients did not have a CPPS diagnosis or were only interested in the diagnostic algorithm but not in the treatment study. Moreover, the low eligibility rate might be attributed to the time lag between initial eligibility screening and trial inclusion. In our study, up to 3 ½ years have passed since the patient's last appointment at the outpatient clinic and the inquiry for the study. Since it was a rather long time, several factors might have affected eligibility: First, many patients were unattainable due to re-locations or other, mostly unknown, reasons. Second, given the natural course of chronic pain, nearly one third of the patients have less symptoms over time or are even symptom-free [47]. Third, patients with CPPS were likely to use other health care services in order to find pain relief [48]. Future trials should strive for a shorter time period between first contact with the patient and trial inclusion. Nevertheless, although the recruitment process faced these challenges, the

intended sample size could be reached underlining the feasibility of the study. The feasibility of the physio- and psychotherapy combination treatment was also supported by the low dropout rates for the intervention in total and for psycho- and physiotherapy separately. These rates were smaller in comparison to the literature [49, 50] and indicated high acceptance of the treatment. Finally, the feasibility is also indicated by the high level of satisfaction expressed by the participants. Satisfaction with the treatment is suggested to be a basic component for carrying out a successful psychotherapeutic and physiotherapeutic treatment [51]. However, directly comparing this study with existing studies is difficult, since, to the best of our knowledge, this is the first study to investigate combined physio- and psychotherapy in patients with CPPS.

While the eligibility rate was still within the interquartile range of examined studies by Gross et al. [46], the willingness-to-participate rate was considerably below the interquartile range. Although the majority of persons perceived research to be very important, the willingness to participate often depends on convenience and whether or not study participation interfered with the daily routine [52]. Moreover, patients are more likely take part in a study if the home-study site distance is short [53]. In our study, perceived lack of time, long distance to study site, and/or no interest were the most common reasons to refuse participation. Our willingness to participate rate would have improved substantial if we had delivered as least some parts of the intervention in a flexible, possible online format. Hence, these barriers should be targeted when designing future studies. One possible solution might be to concept at least some of the treatment sessions as online sessions. Not only do online programmes enable treatments independent of the home-study site distance, but also allow participants to

better integrate the content of the therapy into their daily routine [54]. Furthermore, online programmes provide continuity of care during pandemic situations like the COVID-19 outbreak [55].Taking these adaptations in mind, we deem our combined intervention feasible and accepted by the patients.

Besides delivering feasibility, we also looked at effect sizes in order to explore evaluating feasibility. Several psychometric indicators showed that the intervention group improved in comparison to the control group although only the estimation of effect size measured with the PDI and the PHQ-9 reached significance level. Nevertheless, the intervention seems to be more effective than treatment as usual in terms of reduction of pain disabilities and depressive symptoms. Interestingly, the sequence psychotherapy first, physiotherapy second appears to be more effective than the other way around. Similar findings were observed in patients with chronic neck pain, who had greater effects in pain and disability reduction as well as quality of life when combining psychotherapy with subsequent physiotherapy. The authors conclude, that patients would need the physical performance in which they can apply and train the theoretical content of the cognitive behavioural therapy [56]. We have found that the intervention effects did not differ by gender. One possible explanation could be that women and men with CPPS have similar symptom patterns. Previous studies have shown that both sexes had similar pain intensity levels [57] and that the proportion of mental disorders is elevated in comparison to the general population in both women and men [16]. Hence, with the assumption of symptoms akin, the intervention might have had worked similar for female and male patients with CPPS. Nevertheless, the sex-disaggregated subsamples were small, which might affect the effect sizes [58].

Prior to conducting an RCT, it is important to perform a power calculation to estimate the optimum sample size. For this purpose, the given effect sizes can be used. The Covid-19 pandemic also shows that online formats can be helpful to avoid treatment interruptions and to reach patients from rural areas more easily. An important point is that in addition to the professional groups involved, the patients' perspective should be included in the study design. While this feasibility study focused on acceptance, the next step should be to investigate the efficacy of the treatment with an appropriate design. Future studies should emphasize possible sex differences in order to tailor the interventions more specifically and effectively to the respective target group. To increase generalizability, a multi-centre study would be the best option.

Limitations

Some limitations of the study should be mentioned. The SF-12 showed only a small and non-significant effect. The failure to detect a significant effect might be attributed to the small sample size of the study, but it could also be due to the generic nature of the instrument, which is not precise enough to detect changes in quality of life in patients with CPPS. This phenomenon was observed in patients with chronic low back pain [59] and thus might also be true for patients with CPPS. Usage of a CPPS-specific instrument like the NIH-CPSI [36] instead of generic outcomes might be considered in future trials. Furthermore, this study is a

feasibility study, which included a small, non-sufficient sample for testing the feasibility of the evaluation and for efficacy testing. Due to the small sample, we rather focused on the effect size Cohen's d than on the statistical significance. Although the effect size is more robust in small samples than the p-value, it is not completely unaffected by sample size [58]. Owing to the construction of the study as a monocentric pilot study, allocation to intervention and control group was non-randomized, which might cause variations in the distribution of sample characteristics. However, no significant differences in study characteristics could be detected between the two branches, which does not give support for the presence of bias. Thus, at this stage of research a non-randomized feasibility study seemed reasonable. It provides first hints that a combined physio- and psychotherapy treatment might be beneficial and that the evaluation of the effect using psychometric questionnaires focussing on pain disabilities rather than quality of life is feasible. However, some studies, which administered either physio- or psychotherapy, exist. The German concept reflective respiratory physiotherapy as such has not been tested, but the American Wise-Anderson-Protocol includes similar therapeutic elements. A case series with male patients demonstrated decreased pain intensity and improved quality of life [60]. The psychotherapeutic programme applied in this study was tested with a group of Canadian men showing positive effects in terms of pain intensity, catastrophizing and quality of life [61]. In comparison, the combination of both therapeutic approaches in this study also indicate, amongst other positive effects, that pain and catastrophizing decreased, and quality of life increased. Nonetheless, since existing studies are highly heterogeneous, comparing this study with available literature should be viewed with caution. Furthermore, the absence of a patient perspective in the design of the study may also have an impact on the acceptance of the therapy.

Finally, we would like to state that this study provides valuable insights for further randomized, multicentre studies; not only regarding the acceptance and the effect of the intervention, but also regarding the recruitment process. The first results of a combined physio- and psychotherapeutic treatment for patients with CPPS appear to be promising although some adaptations to the treatment programme had to be made as outlined above. Further testing of this procedure is therefore urgently needed to provide adequate and scientifically based treatment for patients with CPPS.

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Competing Interests

Gesche Ketels declares that she is a co-founder of the Association for Reflective Respiratory Physiotherapy (Verein für Reflektorische Atemtherapie e.V.), which was established in 2000. She has been a freelance lecturer for reflective respiratory physiotherapy for over 15 years. The other authors declare that they have no competing interests.

Author Contributions

Christian. A. Brünahl: Conceptualization, Writing – Review & Editing, Supervision, Project administration, Funding acquisition; ***Susanne G.R. Klotz:*** Investigation, Data Curation, Writing – Original Draft, Visualization; ***Christoph Dybowski:*** Formal analysis, Investigation, Data Curation, Writing – Review & Editing, Visualization; ***Rebecca Albrecht:*** Investigation, Writing – Review & Editing; ***Johanna Höink:*** Resources, Writing – Review & Editing; ***Margit Fisch:*** Resources, Writing – Review & Editing; ***Gesche Ketels:*** Conceptualization, Writing – Review & Editing, Funding acquisition; ***Bernd Löwe:*** Conceptualization, Resources, Writing – Review & Editing, Supervision, Funding acquisition.

Data Sharing Statement

Technical appendix, statistical code, and dataset available upon reasonable request from the corresponding author.

Ethics Statement

This study (reference number PV4801) and the CPPS outpatient clinic, from which the participants were recruited (reference number PV4220), were approved by the Ethics Committee of the Medical Association Hamburg, Germany.

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Table 1: Comparison of demographic and clinical characteristics at baseline

Variable	Intervention group (n = 36)	Control group (n = 24)	p-value
Demographic characteristics			
Female, % (n)	52.8 (19)	58.3 (14)	.67*
Age in years, mean (SD)	48.6 (±14.8)	50.6 (±14.5)	.60‡
Marital status, % (n)•	(n = 35)	(n = 22)	.29†
Single	37.1 (13)	27.3 (6)	
Married	37.1 (13)	45.5 (10)	
Divorced	25.7 (9)	18.2 (4)	
Other	0	9.1 (2)	
Educational level, % (n)•	(n = 28)	(n = 20)	.13†
6 years of secondary school	14.3 (4)	20.0 (4)	
8 years of secondary school	28.6 (8)	55.0 (11)	
High school graduation	53.6 (15)	25.0 (5)	
Other	3.6 (1)	0	
Pain duration in years, mean (SD)	6.2 (4.8)	6.2 (4.8)	.98‡
Psychometric assessments, mean (SD)			
GAD-7	7.9 (5.5)	6.5 (5.1)	.33‡
PCS	23.4 (13.6)	22.9 (16.1)	.90‡
PDI	26.7 (15.2)	26.6 (18.3)	.95‡
PHQ-9	9.9 (5.8)	9.1 (6.9)	.65‡
PHQ-15	11.0 (5.0)	10.3 (6.0)	.63‡
PSQ	0.5 (0.2)	0.5 (0.2)	.78‡
SF-12 PCS	39.5 (8.5)	38.0 (12.0)	.61‡
SF-12 MCS	39.9 (11.9)	40.2 (11.1)	.93‡
SF-MPQ total	18.2 (9.4)	18.6 (12.5)	.89‡
SF-MPQ sen.	13.2 (7.1)	14.6 (8.6)	.52‡
SF-MPQ aff.	5.0 (3.2)	4.0 (4.2)	.33‡
NIH-CPSI total	24.1 (7.4)	23.7 (7.6)	.83‡
Pain subscale	11.3 (3.8)	11.4 (3.7)	.92‡
Urinary subscale	4.7 (2.9)	4.1 (2.7)	.38‡
QoL subscale	8.0 (2.3)	8.2 (2.7)	.85‡

Legend: •assessed at outpatient clinic visit (t1); *Chi²; ‡t-test for independent samples; †Fisher's exact test; GAD-7 = Generalized Anxiety Disorder Screener; NIH-CPSI = Chronic Prostatitis Symptom Index of the National Institutes of Health; PCS = Pain Catastrophizing Scale; PDI = Pain Disability Index; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); PHQ-15 = Patient Health Questionnaire 15 (somatic symptoms); PSQ = Perceived Stress Questionnaire; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ aff. = affective subscale of Short Form McGill Pain Questionnaire; SF-MPQ sen. = sensory subscale of Short Form McGill Pain Questionnaire; SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; SD = standard deviation

Table 2: Treatment satisfaction

	All		Female		Male		Overall comparisons		
							Modules[a]	Sex	Modules*sex
	N	Est. M (SE)	N	Est. M (SE)	N	Est. M (SE)	p (d)	p (d)	p (d)
Overall treatment	25	6.0 (0.2)	14	5.9 (0.3)	11	6.2 (0.3)	0.08 (0.72)	0.37 (0.38)	0.89 (0.10)
Psychotherapeutic module	25	5.4 (0.3)	14	5.1 (0.4)	11	5.6 (0.4)			
Physiotherapeutic module	25	5.9 (0.3)	14	5.6 (0.4)	11	6.1 (0.5)			

Legend

Items: “Would you recommend …?”; scale from 1 = „does not apply at all“ to 7 = “fully applies”;

higher values correspond with higher treatment satisfaction.

Est. M = estimated mean; SE = standard error

[a]Overall treatment vs psychotherapeutic module vs physiotherapeutic module

Table 3: Post-treatment (t6) comparisons between the intervention group and the control group, adjusted for baseline (t2), sex, and the interaction of sex*group

	Intervention group			Control group			Comparison					
Outcome variable	n	Est. mean	SE	n	Est. mean	SE	Mean difference	ES	ES SE	ES CI 95% lower limit	ES CI 95% upper limit	p
SF-12 PCS	22	44.2	1.3	23	41.7	1.3	2.5	0.40	0.3	-0.19	0.99	0.18
SF-12 MCS	22	42.8	1.9	23	41.4	1.9	1.4	0.15	0.3	-0.43	0.74	0.61
PDI	22	18.4	2.3	22	26.5	2.4	-8.1	**-0.73**	0.3	-1.34	-0.12	**0.02**
NIH-CPSI total	22	18.6	1.5	23	20.8	1.5	-2.2	-0.31	0.3	-0.90	0.28	0.30
Pain subscale	22	8.6	0.8	23	9.5	0.8	-0.8	-0.22	0.3	-0.81	0.37	0.46
Urinary subscale	22	3.7	0.4	23	3.8	0.4	-0.1	-0.04	0.3	-0.63	0.54	0.88
QoL subscale	22	6.4	0.5	23	7.5	0.5	-1.2	-0.50	0.3	-1.10	0.09	0.10
SF-MPQ total	22	12.3	1.7	22	15.6	1.7	-3.2	-0.40	0.3	-1.00	0.20	0.19
SF-MPQ sensory	22	9.7	1.2	22	11.2	1.2	-1.5	-0.27	0.3	-0.86	0.33	0.38
SF-MPQ affective	22	2.7	0.6	22	4.2	0.6	-1.5	-0.55	0.3	-1.16	0.05	0.08
PCS	22	14.7	1.8	22	19.5	1.8	-4.8	-0.56	0.3	-1.17	0.04	0.07
PHQ-9	22	6.9	0.9	22	9.5	0.9	-2.6	**-0.62**	0.3	-1.23	-0.02	**0.04**
GAD-7	22	5.7	0.9	22	6.5	0.9	-0.9	-0.21	0.3	-0.81	0.38	0.48
PHQ-15	22	9.9	0.8	21	9.8	0.8	0.2	0.04	0.3	-0.56	0.64	0.89
PSQ	22	0.4	0.0	22	0.5	0.0	-0.0	-0.14	0.3	-0.74	0.45	0.64

Legend

p-values <.05 and corresponding ES are presented in bold
Est. = estimated; SE = standard error; ES = effect size Cohens' d; ES
SE= standard error of the effect size;
ES CI = confidence interval of the effect size
SF-12 PCS = 12-Item Short Form

Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ sensory = sensory subscale of the Short Form McGill Pain Questionnaire; SF-MPQ affective = affective subscale of the Short Form McGill Pain Questionnaire; PCS = Pain Catastrophizing Scale; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); GAD-7 = Patient Health Questionnaire Generalized Anxiety Disorder Screener; PHQ-15 = Patient Health Questionnaire 15 (severity of somatic symptoms); PSQ = Perceived Stress Questionnaire

Table 4: Sex-dependent post-treatment (t6) comparisons between the intervention group and the control group

	Female patients								Male patients										
	Intervention group			Control group			Comparison		Intervention group			Control group			Comparison		Overall		
Outcome variable	n	Est. mean	SE	n	Est. mean	SE	Mean diff.	ES	n	Est. mean	SE	n	Est. mean	SE	Mean diff.	ES	ES diff.	p main effect sex	p interaction sex*group
SF-12 PCS	10	45.6	1.9	14	43.0	1.6	2.6	0.44	12	42.7	1.7	9	40.4	2.0	2.3	0.39	0.05	0.13	0.94
SF-12 MCS	10	41.0	2.9	14	39.9	2.4	1.1	0.12	12	44.6	2.6	9	42.8	3.0	1.8	0.20	-0.08	0.24	0.90
PDI	10	18.8	3.5	13	26.4	3.0	-7.6	-0.69	12	18.0	3.2	9	26.6	3.7	-8.6	-0.79	0.09	0.92	0.88
NIH-CPSI total	10	19.5	2.2	14	19.9	1.9	-0.4	-0.05	12	17.7	2.0	9	21.8	2.3	-4.1	-0.59	0.53	0.97	0.38
Pain subscale	10	8.9	1.2	14	8.9	1.0	0.0	0.01	12	8.3	1.1	9	10.0	1.2	-1.7	-0.46	0.47	0.78	0.44
Urinary subscale	10	4.3	0.7	14	3.9	0.6	0.4	0.20	12	3.0	0.6	9	3.7	0.7	-0.6	-0.29	0.50	0.23	0.41
QoL subscale	10	6.4	0.7	14	7.1	0.6	-0.8	-0.34	12	6.3	0.7	9	7.9	0.8	-1.6	-0.68	0.34	0.61	0.58
SF-MPQ total	10	12.5	2.5	13	15.6	2.2	-3.1	-0.39	12	12.2	2.3	9	15.6	2.6	-3.4	-0.43	0.04	0.93	0.94
SF-MPQ sensory	10	10.4	1.8	13	11.3	1.6	-1.0	-0.17	12	9.1	1.6	9	11.2	1.9	-2.1	-0.37	0.20	0.66	0.74
SF-MPQ affective	10	2.4	0.9	13	4.2	0.7	-1.8	-0.67	12	3.0	0.8	9	4.3	0.9	-1.3	-0.47	-0.20	0.66	0.75
PCS	10	12.6	2.7	13	19.7	2.3	-7.2	-0.86	12	16.8	2.4	9	19.2	2.8	-2.4	-0.29	-0.57	0.48	0.37
PHQ-9	10	6.9	1.3	13	10.0	1.1	-3.1	-0.75	12	6.9	1.2	9	9.0	1.4	-2.1	-0.52	-0.23	0.70	0.70
GAD-7	10	5.5	1.3	13	5.5	1.1	0.0	0.00	12	5.8	1.1	9	7.5	1.3	-1.7	-0.43	0.43	0.38	0.48
PHQ-15	10	10.3	1.1	12	9.7	1.0	0.6	0.18	12	9.5	1.0	9	9.8	1.2	-0.3	-0.09	0.27	0.74	0.67
PSQ	10	0.4	0.0	13	0.5	0.0	0.0	-0.29	12	0.5	0.0	9	0.5	0.0	0.0	0.00	-0.29	0.80	0.64

Legend:
SE = standard error; Est. = estimated; diff. = difference; ES = effect size Cohen's d
SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ sensory = sensory subscale of the Short Form McGill Pain Questionnaire; SF-MPQ affective = affective subscale of the Short Form McGill Pain Questionnaire; PCS = Pain Catastrophizing Scale; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); GAD-7 = Patient Health Questionnaire Generalized Anxiety Disorder Screener; PHQ-15 = Patient Health Questionnaire 15 (severity of somatic symptoms); PSQ = Perceived Stress Questionnaire

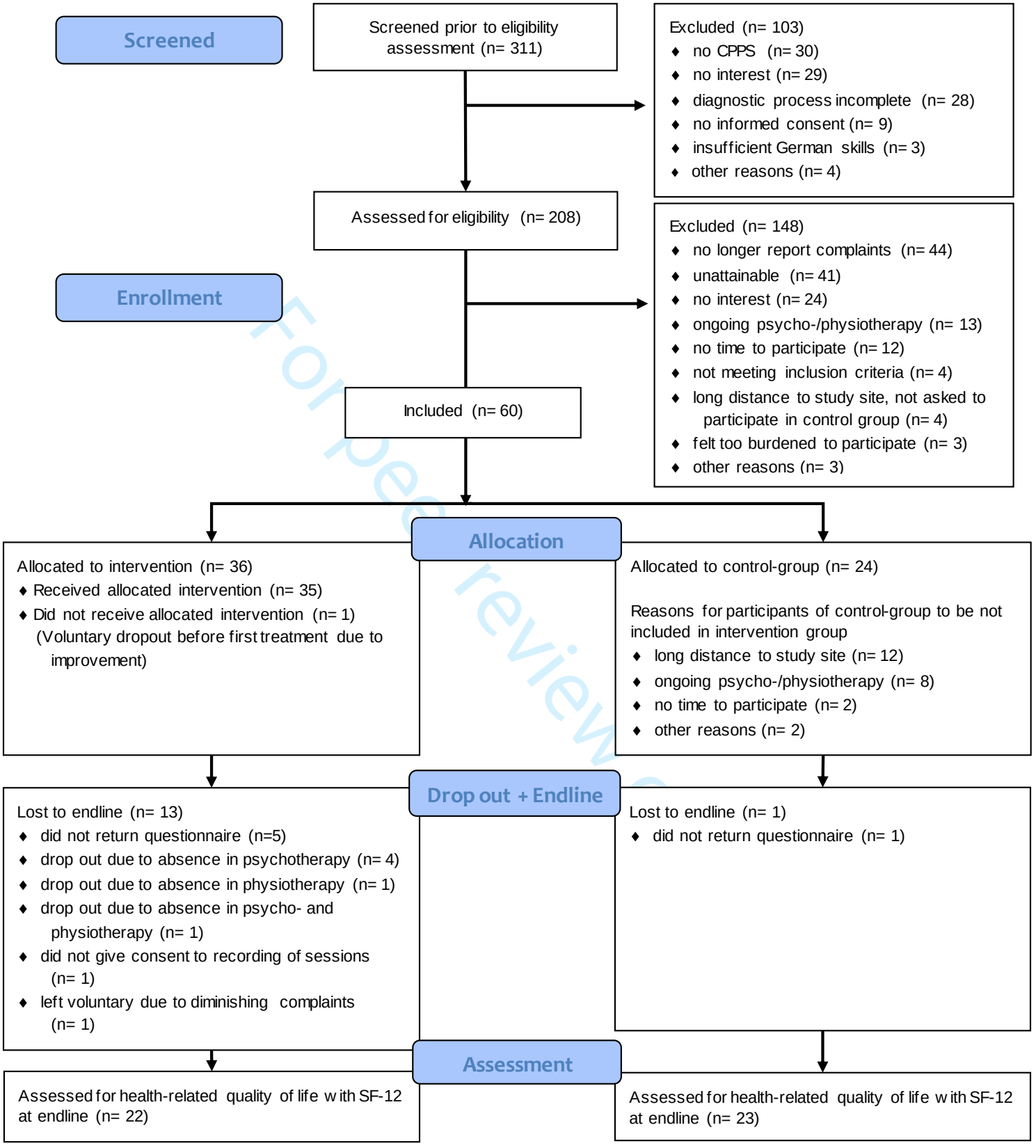
Figure 1: Flow of participants

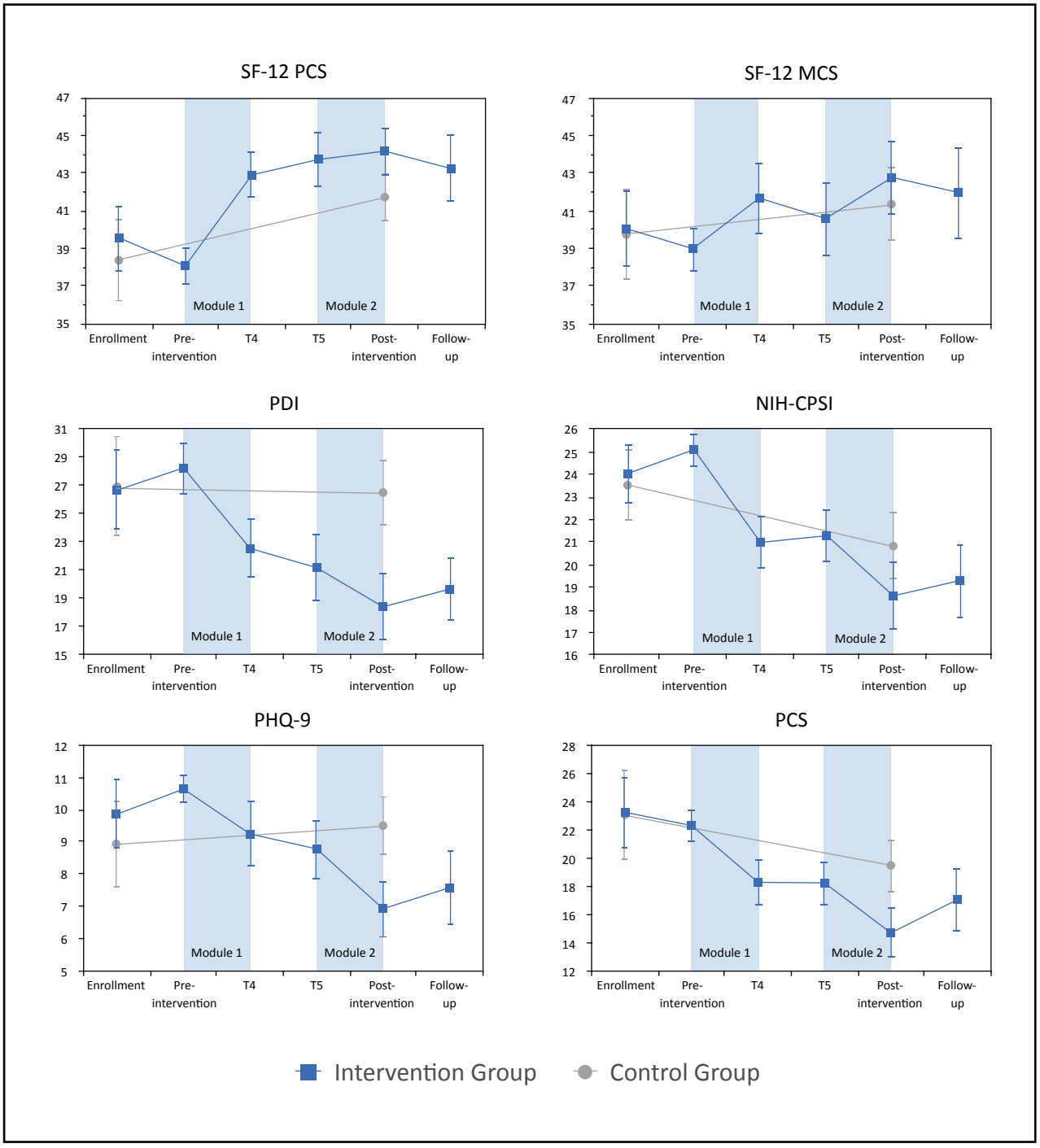
Legend: SF-12: 12-Item Short Form Health Survey

Source: Eldridge et al. (2016)

Figure 2: Course of important outcome variables in the intervention and the control group

Legend: SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; PHQ-9 = Patient Health Questionnaire 9; PCS = Pain Catastrophizing Scale




SF-12 PCS
SF-12 MCS
PDI
NIH-CPSI
PHQ-9
PCS
Module 1
Module 2
Enrollment
Pre-intervention
T4
T5
Post-intervention
Follow-up
Intervention Group
Control Group

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility trial in the title	1
	1b	Summary of pilot trial design, methods, results, and conclusions	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for pilot trial	5-6
	2b	Specific objectives or research questions for pilot trial	5-6
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	6-7
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	7-8
	4b	Settings and locations where the data were collected	6-7
	4c	How participants were identified and consented	7-8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8-9
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	9-10
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	N/A
Sample size	7a	Rationale for numbers in the pilot trial	N/A
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	N/A
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	N/A
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	N/A
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to	N/A

		interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	Figure 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	12
	14b	Why the pilot trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	Figure 1
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	12-14 Tables 2-4
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	15-19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	16-17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	15-17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	18-19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	7
Protocol	24	Where the pilot trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	20
	26	Ethical approval or approval by research review committee, confirmed with reference number	7

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.

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Trials

STUDY PROTOCOL Open Access

Combined Cognitive-Behavioural and Physiotherapeutic Therapy for Patients with Chronic Pelvic Pain Syndrome (COMBI-CPPS): study protocol for a controlled feasibility trial

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Abstract

Background: Chronic pelvic pain syndrome (CPPS) is a pain condition perceived in the pelvic area for at least 6 months. While evidence of the aetiology and maintenance of CPPS is still unclear and therapy options are rare, there is preliminary evidence for the efficacy of cognitive behavioural therapy and physiotherapy. However, an integrated treatment has not yet been studied. The primary aim of this study is therefore to test the feasibility of combined psychotherapy and physiotherapy for female and male patients with CPPS. The secondary aim is to explore changes in patient-relevant and economic outcomes compared to a control group.

Methods: A feasibility study with a crossover design based on the principles of a 'cohort multiple randomized controlled trial' will be conducted to test a combined therapy for patients with CPPS. The study will consist of two consecutive treatment modules (cognitive behavioural group psychotherapy and physiotherapy as individual and group sessions), which will be applied in varying order. The modules will consist of nine weekly sessions with a 4-week break between the modules. The control group will undergo treatment as usual. Study subjects will be recruited from the interdisciplinary outpatient clinic for CPPS at the University Medical Center Hamburg-Eppendorf. Thirty-six patients will be assigned to the intervention, and 18 patients will be assigned to the control group. The treatment groups will be gender homogeneous. Feasibility as the primary outcome will be analysed in terms of the demand, acceptability, and practicality. Secondary study outcomes will be measured using validated self-rating-scales and physical examinations.

Discussion: To the best of our knowledge, this study is the first to investigate the feasibility of combined psychotherapy and physiotherapy for patients with CPPS. In addition to testing feasibility, the results can be used for the preliminary estimation of therapeutic effects. The results from this study will be used to generate an enhanced therapeutic approach, which might be subject to further testing in a larger study.
(Continued on next page)

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(Continued from previous page)

Trial registration: German Clinical Trials Register, DRKS00009976. Registered on 15 March 2016. ISRCTN, ISRCTN43221600. Registered on 10 May 2016.

Keywords: Chronic pelvic pain syndrome, Chronic pain, Cognitive behavioural therapy, Group psychotherapy, Physical therapy modalities, Feasibility studies

Background

Chronic pelvic pain syndrome (CPPS) can be described as an intermittent or constant pain condition in the pelvic area that has persisted for at least 6 months without an obvious pathology that accounts for the pain [1]. It is associated with physical symptoms suggestive of gastroenterological, urogenital, and/or sexual dysfunction [1–3] as well as with psychopathological symptoms and a reduced health-related quality of life [1, 4–15]. Psychological correlates are also emphasized by clinical phenotyping systems, such as UPOINT [16]. Thirty-four to 37% of the patients with CPPS have positive findings in the UPOINT domain 'psychosocial dysfunction'. Furthermore, 53–64% of the patients have findings in the 'tenderness of muscles' domain [17, 18], suggesting that psychotherapy and physiotherapy might be important in the treatment of patients with CPPS.

CPPS is a common pain condition with international general population prevalence rates ranging between 4 and 25% in women [8, 19–21] and between 2 and 18% in men [22–24].

Although CPPS is common, the aetiology and maintenance of CPPS are still largely unknown [25–29] and the successful management of this pain syndrome remains challenging [30, 31]. Several single-track medical and non-medical treatment strategies have failed to be sufficient [31, 32]. Therefore, a multidisciplinary approach combining medical, psychotherapeutic, and physiotherapeutic treatment strategies is recommended [1, 18, 33]. However, some psychotherapeutic and physiotherapeutic treatment strategies have shown promising effects. Cognitive behavioural therapy (CBT) strategies seem to reduce pain and symptom severity as well as increase the quality of life [34–36]. Myofascial physiotherapy techniques alone or in combination with breathing and relaxation techniques appear to be effective for treating urinary and sexual symptoms, pain, and quality of life [37–41].

Objectives

Regarding the advocacy for multimodal therapy established in the guidelines of the European Association of Urology (EAU) [1], there is an urgent need to examine combined interventions for patients with CPPS. However, due to constraints of resources, not all interventions can be tested for efficacy and effectiveness. In this case, a feasibility study can be used to decide whether a treatment method is worth further investigation and whether changes should be applied to the intervention [42].

Therefore, the primary aim of this study is to explore the feasibility of a combined psychotherapeutic and physiotherapeutic treatment for both female and male patients with CPPS. The results from this study will be used to generate an enhanced therapeutic approach, which might be subject to further testing. Additionally, the secondary objective of this study is to determine the preliminary indicators for the efficacy of this treatment programme regarding urological symptoms, psychological and physical correlates, health-related quality of life, and healthcare utilization. The results can be used to calculate the optimal sample size for a randomized controlled trial (RCT).

Methods/design

Study design

This study will be conducted based on the principles of a 'cohort multiple randomized controlled trial' (cmRCT) proposed by Relton et al. [43]. In this pragmatic study design, an observational cohort of subjects with the parameter of interest will be recruited and evaluated on a regular basis. For a randomized controlled trial, random subjects from all eligible subjects in the cohort are allocated to the intervention group, while allocation to the control group is not randomized [43].

The feasibility study is embedded in the Interdisciplinary Research Platform Chronic Pelvic Pain Syndrome (CPPS), which was initiated in 2012 at the University Medical Center Hamburg-Eppendorf to obtain insight into the somatic and psychological aspects in CPPS and to develop treatment strategies for these patients. In cooperation with different medical specialties (e.g. psychosomatic medicine, urology, gynaecology, and physiotherapy), a specialized outpatient clinic for patients with CPPS was implemented [5]. The assessment at this outpatient clinic includes a diagnosis of CPPS according to the EAU guidelines [1]. People diagnosed with CPPS constitute the observational cohort, from which subjects for this study will be recruited.

The treatment will consist of a combination of cognitive behavioural psychotherapy and physiotherapy based on an aetiological model developed especially for patients with

CPPS [6]. Psychotherapeutic and physiotherapeutic treatment modalities will be applied as consecutive modules, and both sequences will be tested (psychotherapy followed by physiotherapy vs physiotherapy followed by psychotherapy). The intervention will therefore consist of two branches, one starting with psychotherapy and the other starting with physiotherapy. For a detailed overview of the study design, see Fig. 1.

Sample

Study subjects will be recruited from the observational cohort consisting of all patients assessed at the interdisciplinary outpatient clinic for CPPS at the University Medical Center Hamburg-Eppendorf.

The following criteria will be applied to identify eligible patients in the observational cohort: CPPS diagnosis according to the EAU guidelines [1] and classification of the International Association for the Study of Pain [44], informed consent, sufficient German language skills, age > 18 years, and score ≤ 40 for the mental or physical scale of the 12-Item Short-Form Health Survey (SF-12) [45]. Exclusion criteria are delusional disorders, substance dependence (except nicotine or pain medication), acute suicidal tendencies, planned absences over the treatment period, and current psychotherapy or physiotherapy.

The targeted sample size for the study is 54 participants. Thirty-six participants will be assigned to the intervention group and 18 to the control group. This sample size allows for evaluation of the study in terms of feasibility and can be used to estimate therapeutic effects (pre–post and between groups). Although the sample size is not sufficient to prove the efficacy of the combined treatment programme, the results of the study can be used to calculate the sample size for a subsequent RCT.

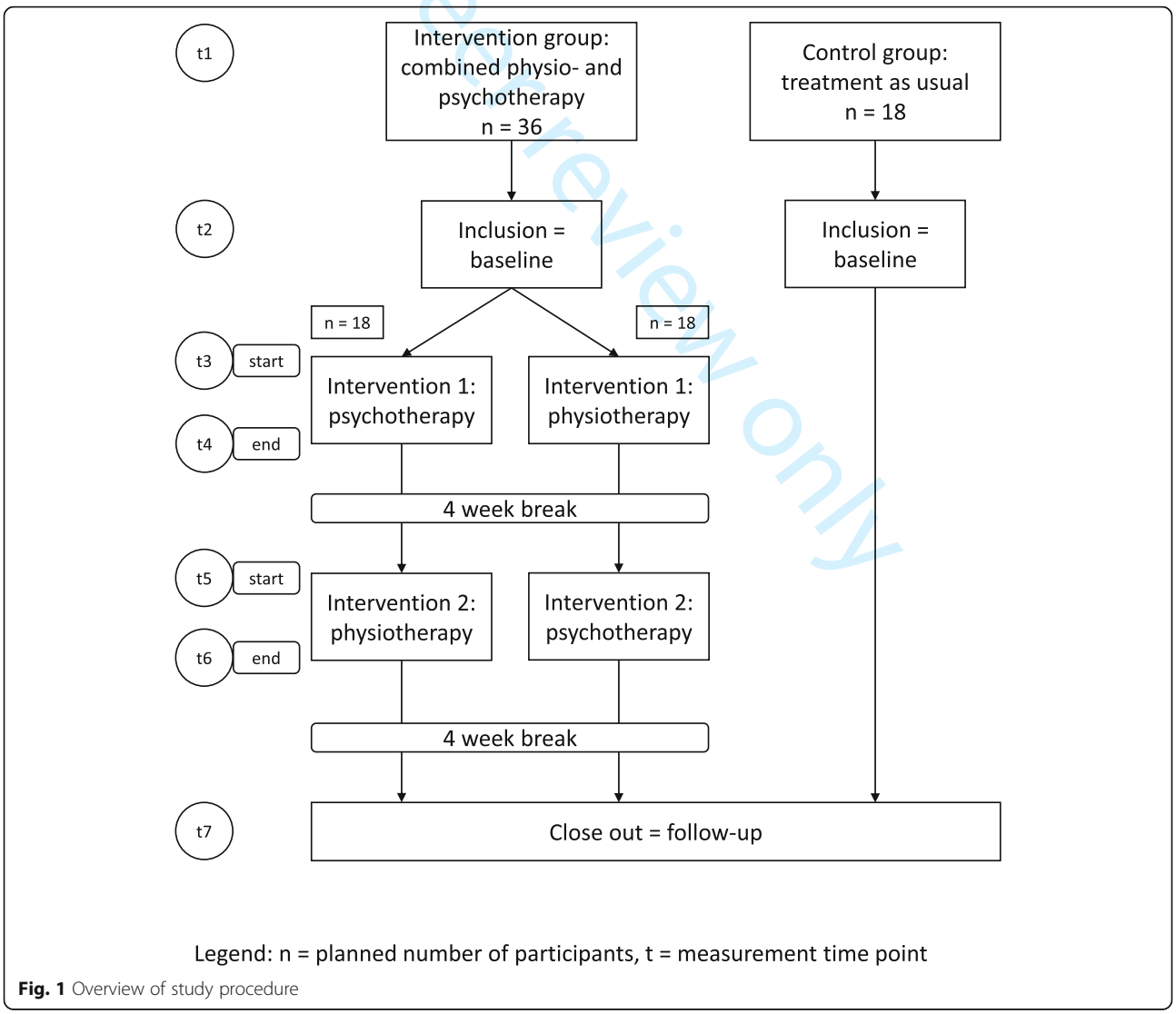

Fig. 1 Overview of study procedure

Assignment of eligible subjects to treatment and control groups will not be randomized; instead, it will be determined by the ability to regularly participate in the treatment sessions at the University Medical Center Hamburg-Eppendorf. Regular participation is defined as a maximum miss of four of the 18 treatment sessions. The assignment to one of the two treatment sequences (starting with psychotherapy vs starting with physiotherapy) will be randomized.

Procedure

In a first step, all eligible patients who were examined in the interdisciplinary CPPS outpatient clinic since 2012 (time point t1), and are thus part of the observational cohort, will be identified and assigned to either the treatment group or the control group. Detailed information about the pilot study will be sent to these patients by postal mail, whereby the informed consent signed previously by patients for the assessment at the outpatient clinic facilitates contacting them for future research. Patients willing to participate in either the treatment group or the control group will undergo a telephone interview to re-examine eligibility in case changes have occurred since their visit to the outpatient clinic and to answer open questions about the study. After inclusion, participants will receive two copies of the informed consent document, the final time schedule and a set of questionnaires (time point t2; see Instruments for a detailed description). Participants of the treatment group will also be contacted by a physiotherapist to schedule an examination appointment. Patients who do not meet inclusion criteria will be informed by telephone and will receive support regarding alternative treatment options, if requested. Patients' reasons for non-participation, if given, will be documented. In addition, patients who do not respond to the initial letter will also be contacted by telephone.

Further measurements will be conducted at the beginning (t3) and end of the first intervention module (t4) and at the beginning (t5) and the end of the second intervention module (t6) as well as 4 weeks after finishing the second intervention module (t7). The study procedure is in line with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement 2013 [46] (see also Additional file 1: SPIRIT checklist). Figure 2 displays the schedule of enrolment, interventions, and assessments according to the SPIRIT statement.

Intervention group

The intervention will consist of two consecutive treatment modules (cognitive behavioural group psychotherapy and physiotherapy as both group and individual sessions). A 4-week break is scheduled between the two modules. The intervention group has two branches; therefore, subjects will start with either one of the modules described in the following. A group size of nine patients for the psychotherapy as well as for the physiotherapy group sessions is regarded as adequate even in the event of drop-outs. This group size also reflects the maximal number of patients allowed in a CBT group in the German healthcare system [47]. The groups will be gender homogeneous because CPPS is characterized by symptoms in an intimate body region potentially associated with shame [48]. With a targeted sample size of 36 participants in the intervention and a group size of nine in the therapeutic sessions, the overall intervention group will consist of four therapeutic groups, two with only male participants and two with only female participants. One group of each gender will start with either psychotherapy or physiotherapy, resulting in four treatment groups in the intervention group.

Cognitive behavioural psychotherapy

The psychotherapeutic intervention will consist of nine weekly group sessions, each lasting 90 minutes. The sessions will be based on the following pattern: group discussion of assignments (behaviour analysis, reading a particular chapter from the patient workbook described in the following), progressive muscle relaxation (PMR) according to Jacobson [49], session-specific theory, consolidation of the specific theory through group work, concluding round, and new assignments. For a detailed overview of the CBT, see Table 1. Each session will be held by a trained and skilled CBT therapist (licensed psychotherapist) and a co-therapist (resident physician); one will be male and the other female. In order to increase generalizability we have a pool of five therapists (three female, two male) who can deliver the study intervention. All therapists will receive in-house training especially for the study and will be supervised by one specialist in CBT. During the initial session, patients will receive a printed version of the patient workbook containing theoretical background information, assignments, and repeated questionnaires regarding their symptoms for the self-evaluation of their course.

The patient workbook for cognitive behavioural group psychotherapy has been designed by members of our study group, and is based on the work of Tripp, Nickel, and Mullins [50, 51] who developed a treatment rationale for individual therapy and demonstrated its feasibility and yielded first indicators of its efficacy [35]. Through cooperation with the Canadian workgroup, we were able to translate, expand, and adapt their patient workbook [51] to the needs of our study and the German healthcare system. Key topics for the cognitive behavioural intervention are as follows:

		STUDY PERIOD					
	Outpatient clinic	Enrolment	Post-allocation				Close-out
			Start intervention 1	End intervention 1	Start intervention 2	End intervention 2	4-week follow-up
TIMEPOINT	t_1	t_2	t_3	t_4	t_5	t_6	t_7
ENROLMENT:							
Eligibility screen		X					
Informed consent		X					
Allocation		X					
INTERVENTIONS:							
Psychotherapy + Physiotherapy			←	→	←	→	
Physiotherapy + Psychotherapy			←	→	←	→	
Control group							
ASSESSMENTS:							
Sociodemographic data, case history	X						
Examination by a physical therapist	X	X			X		X
Health Care Utilization Questionnaire	X	X	X	X	X	X	X
Urological symptoms (NIH-CPSI)	X	X	X	X	X	X	X
Health-related quality of life (SF-12)	X	X	X	X	X	X	X
Pain perception (SF-MPQ)	X	X	X	X	X	X	X
Impact of pain on daily activities (PDI)	X	X	X	X	X	X	X
Catastrophizing thinking (PCS)	X	X	X	X	X	X	X
Perceived stress (PSQ)	X	X	X	X	X	X	X
Depressive symptoms (PHQ-9)	X	X	X	X	X	X	X
Somatic symptom severity (PHQ-15)	X	X	X	X	X	X	X
Generalized anxiety (GAD-7)	X	X	X	X	X	X	X
Goal attainment (GAS)*				(X)		(X)	
Patient satisfaction			X	X	X	X	

Fig. 2 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) schedule of enrolment, interventions, and assessments [46]. Legend: *GAD* = Generalized Anxiety Disorder Scale; *GAS* = Goal Attainment Scaling; *NIH-CPSI* = Chronic Prostatitis Symptom Index of the National Institute of Health; *PCS* = Pain Catastrophizing Scale; *PDI* = Pain Disability Index; *PHQ* = Patient Health Questionnaire; *PSQ* = Perceived Stress Questionnaire; *SF-MPQ* = Short-Form McGill Pain Questionnaire; *SF-12* = 12-Item Short-Form Health Survey; t = time point; * = only after the physical therapy intervention module (either at t4 or at t6)

Table 1 Overview of cognitive behavioural group psychotherapy sessions

Session	Content	Modality
1	Introduction to the programme; issuing of the patient workbook; overview of key topics; introduction to PMR	Group (90 min)
2	Group discussion/debriefing of Chapter 1 of the patient workbook; exercise of PMR; behaviour analysis	Group (90 min)
3	Group discussion/debriefing of Chapter 2 of the patient workbook; exercise of PMR; theory: catastrophizing cognitions; behaviour analysis	Group (90 min)
4	Group discussion/debriefing of Chapter 3 of the patient workbook; exercise of PMR; theory: negative self-talk; behaviour analysis	Group (90 min)
5	Group discussion/debriefing of Chapter 4 of the patient workbook; exercise of PMR; theory: influence of social relationships (Part 1); modification of 'I-message'; behaviour analysis (focus: social interaction)	Group (90 min)
6	Group discussion/debriefing of Chapter 5 of the patient workbook; exercise of PMR; theory: influence of social relationships (Part 2)/asking for support; modification of listening skills; behaviour analysis	Group (90 min)
7	Group discussion/debriefing of Chapter 6 of the patient workbook; exercise of PMR; theory: coping strategies (Part 1)/role of positive self-messages; behaviour analysis	Group (90 min)
8	Group discussion/debriefing of Chapter 7 of the patient workbook; exercise of PMR; theory: coping strategies (Part 2); activity and inactivity/recognizing avoidance behaviour; behaviour analysis	Group (90 min)
9	Group discussion/debriefing of Chapter 8 of the patient workbook; exercise of PMR; assessment of changes during the programme; revision of key topics	Group (90 min)

min minutes, *PMR* progressive muscle relaxation

- coping with catastrophizing cognitions,
- reduction of avoidance behaviour/increase of physical activity,
- development of coping strategies, and
- enhancing social support.

Furthermore, behaviour analysis also plays a key role in the programme. As group therapy facilitates the acquisition of new behaviour patterns [52], behaviour changes are addressed in the group setting. To increase the possibility of implementation into the German healthcare system we adapted the workbook to a group context.

Physiotherapy

Following the structure of the psychotherapeutic intervention, the physiotherapeutic approach is also designed in nine weekly units. However, unlike the sessions in the psychotherapy, only units 1, 5, and 9 are group treatments, while the others are designed as individual appointments. The group sessions will last 90 minutes each, and the individual sessions will last 60 minutes except for the seventh unit, which will last 90 minutes and include treatment as well as feedback and reflection about the achievement of patients' goals. Because of the more intense activity during the individual treatment and framework of ambulatory physiotherapy in the German healthcare system [53], a shorter duration was chosen in the single sessions.

The treatment is based on the Wise–Anderson Protocol, an American physiotherapeutic intervention for patients with CPPS combining trigger point therapy, a specific breathing technique, relaxation, and self-management [41, 54]. A German concept that acknowledges most of the elements of the American Wise–Anderson Protocol is Reflektorische Atemtherapie® [55, 56]. The German name of the concept is a registered trademark, and the English translation 'reflective respiratory physiotherapy' is from Zalpour [57]. This therapy aims to regulate psycho-physical coherences using the respiratory system. Specific stimuli of the connective tissue, muscles and tendons, joints, and periosteum are intended to influence the involuntary breathing and diaphragm activity. Hence, the aim is not only to improve the regulation of muscle tone and mobility, but also to affect the internal organs and pelvic floor through enhanced diaphragm mobility [58]. Positive effects of reflective respiratory physiotherapy were found in a study with patients who had chronic obstructive pulmonary disease [59].

The programme will contain the following elements [58, 60]:

- Education about the anatomy and function of the musculoskeletal system and posture with an emphasis on the pelvic floor and diaphragm, the influence of stress on the muscle tone and stiffness of fasciae, and the importance of self-management and adherence to a home exercise programme.
- Application of heat in the form of 'hot towels' (hot water-soaked towels) at the beginning of the therapy to relax muscles and joints, stimulate the circulation, and prepare the tissue for the following techniques.
- Manual techniques for all structures of the musculoskeletal system to mobilize joints and release fasciae with stretching and relaxing muscles.
- Specific therapeutic movements with partially uncomfortable or painful stimuli that influence the respiratory system and the diaphragm reflectively,

affecting the vegetative nervous system and muscle tone.
- Instruction of the patient to self-management and home exercises based on yoga to strengthen and stretch muscles, improve posture and body perception, and sense breathing activity.

In the individual sessions, subjects will be treated according to their individual findings with 'hot towels', manual techniques, and specific therapeutic movements. In addition, home exercises will be taught. During the group sessions, the focus will be on home exercises and self-management together with education and information. Similar to the psychotherapeutic group sessions, the physiotherapy group sessions will be hosted by two physiotherapists, one male and one female. Table 2 presents a scheme for the procedure and content of the physiotherapeutic intervention.

Control group

Allocation to the control group will not be randomized; instead, this will be determined by the ability to participate in the intervention occurring at the University Medical Center Hamburg-Eppendorf. It was considered difficult for patients outside the greater Hamburg area to participate; therefore, they will be allocated to the control group. The control group will not receive any specific intervention as part of the study; nonetheless, patients can seek treatment as usual from their local healthcare provider. Assessment of the control group will be done at two time points; first, at time point t2, which is the enrolment time; and second, at time point t7, which is 4 weeks after the intervention group has finished the second intervention module. The results of these measurements will be compared with the results of the intervention group to gather initial insight into the efficacy of the intervention compared to treatment as usual.

Instruments

The assessment at our interdisciplinary CPPS outpatient clinic constitutes the measurement time point t1. This involves collection of socio-demographic data and the case history, an examination by a physiotherapist, and completion of psychometric questionnaires used in this study. For an overview of the instruments used in this study, see Fig. 2.

Feasibility will be operationalized using information from the participants, therapists, and those involved in organization of the study. Information from participants will include the response rate to study invitation, willingness to participate, and reasons for not participating as indicators of demand. Practicality will be operationalized in terms of the time and personnel expenditures. Attendance at and satisfaction with physiotherapy and psychotherapy sessions, the number of drop-outs and adverse events, and the amount of missing data in the questionnaires of the workbook will function as indicators of acceptability. To assess satisfaction, we developed questionnaires using 7-point Likert scales. Subjects will be asked to rate each psychotherapeutic and physiotherapeutic session, including the accompanying study materials, each whole treatment module (psychotherapy or physiotherapy), and overall contentment with the combination of psychotherapy and physiotherapy. The questionnaires cover therapeutic and organizational aspects.

The secondary objectives of the feasibility study will be measured using the following instruments:

Table 2 Overview of physiotherapy sessions

Session	Content	Modality
1	Relationship between muscle tension, stress, and pain; awareness of tension and relaxation of the pelvic floor muscles; instruction of home exercises/self-management; goal attainment scaling	Group (90 min)
2	Reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
3	Reflection of the past sessions; reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
4	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
5	Reflection of the past group session; instruction of home exercises/self-management	Group (90 min)
6	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
7	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
	Feedback for the individual sessions; evaluation of and reflection on goal attainment; self-management	Single (30 min)
8	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
9	Evaluation of and reflection on goal attainment; self-management; home exercises; feedback and conclusion	Group (90 min)

min minutes

- The health-related quality of life will be assessed using the SF-12 [45], which has been demonstrated as reliable and valid in clinical and population-based samples [61, 62].
- The Chronic Prostatitis Symptom Index of the National Institute of Health (NIH-CPSI) [63] is considered the criterion standard for assessing urological symptom severity in CPPS in the EAU guidelines [1]. The German version with good psychometric properties [64] will be applied in this study. Since the original NIH-CPSI was designed for male patients, a modified version for female patients also exists [65].
- The German version [66] of the Short-Form McGill Pain Questionnaire (SF-MPQ) [67] will be used to assess pain perception.
- The impact of pain on the ability to participate in essential life activities will be measured with the Pain Disability Index (PDI) [68, 69], a valid and reliable [70] instrument.
- Pain catastrophization will be assessed with the aid of the Pain Catastrophizing Scale (PCS) [71], which has been shown to have good psychometric properties [72].
- To quantify the psychological symptom burden, three subscales of the German version of the Patient Health Questionnaire (PHQ-D) [73] with good psychometric characteristics [74–76] will be applied: the PHQ-9 for measuring depressive symptoms [77], the PHQ-15 for measuring the severity of somatic symptoms [78], and the Generalized Anxiety Disorder Scale (GAD-7) [76, 79] for measuring symptoms of generalized anxiety.
- The reliable and valid [80] German short version [81] of the Perceived Stress Questionnaire (PSQ) [82] will be used to assess subjectively experienced stress.
- Assessment of tender and trigger points in the abdominal wall, bottom, thighs, and pelvic floor is done with external and internal manual palpation. Although the reliability of manual palpation is variable [83, 84], it is essential in finding painful points in the muscles [85–87]. In female subjects, internal palpation is done via the vagina and rectum; in male subjects, internal palpation is done via the rectum. Prior to this examination, patients gave written informed consent to internal palpation.
- Participants set their individual therapy goals on the participation level of the International Classification of Functioning, Disability and Health [88] in the first physiotherapeutic group session and evaluate them in the last group treatment using the reliable and valid [89–92] Goal Attainment Scaling (GAS) [93].
- To assess healthcare utilization, we are using the Health Care Utilization Questionnaire, which is a modified version of the Client Socio-Demographic and Service Receipt Inventory—European Version [94] and was developed by the Institute of Health Economics and Health Services Research of the University Medical Center Hamburg-Eppendorf.

Data management and analysis

After completion of data collection, raw data will be entered in prepared electronic databases and merged with the electronically captured data. The accuracy of data will be checked by two independent researchers. Data saving and storage will be performed in accordance with the German regulation of Good Clinical Practice [95].

In addition to the quantitative data, feasibility will be analysed using qualitative data, such as answers to open questions in the satisfaction questionnaires and verbal information.

Descriptive statistics will be used to summarize the sample characteristics (e.g. sex, age, and symptom duration) and two-tailed independent *t*-tests will be used to test for significant differences between the intervention and control groups at enrolment (t2).

Subjects will be analysed on an intention-to-treat basis. To examine the course of the symptoms, related variables will be analysed using the pre–post point estimate comparisons, variability estimates, and 95% confidence intervals. The controlled study design allows for within-group as well as between-group comparisons. Paired-sample *t*-tests will be used for within-group comparisons, while the independent *t*-test will be used for between-group comparisons.

The significance level for all *t*-tests will be set at $p < 0.05$.

The analyses of the course of the symptom-related variables will function as estimates of the effect sizes, while effect estimates can be obtained for physiotherapy and psychotherapy separately as well as the overall effect estimates. These estimates can be used to determine the optimal sample size for a subsequent RCT with a normally distributed sample; hence, parametric tests will be applied as statistical procedures in the feasibility study. Factors influencing therapy success will also be examined.

Statistical analyses will be performed with IBM SPSS Statistics, Version 24 (IBM, Armonk, NY, USA).

Discussion

This article describes the research protocol for a controlled feasibility study of a combination of psychotherapeutic and physiotherapeutic treatments for patients with CPPS. The study will use an interdisciplinary short-term group intervention consisting of psychotherapy and physiotherapy for testing feasibility of the

combined intervention as well as providing the first indicators of efficacy.

The group assignment will be based on the ability of regular participation in the intervention which might lead to selection bias. However, we deemed regular attendance important for the positive effect of the whole intervention programme, and as the complete intervention will last 22 weeks (each intervention module has a duration of 9 weeks with a 4-week break in between) it will require a great concession in terms of time. Participants will not only have a weekly appointment at University Medical Center Hamburg-Eppendorf, they will also have to prepare the psychotherapeutic sessions by reading the workbook chapters and completing the respective questionnaires. It is unclear whether patients will comply with these requirements so that they will be prepared enough to follow and understand the content of the single psychotherapeutic sessions. Moreover, it is expected that at least some subjects will miss one or more sessions due to shift work, unplanned vacations, or other reasons. This might result in difficulties in understanding the content of the subsequent sessions, influencing the effect of the intervention. However, the subjects will have manuals for both the psychotherapy and physiotherapy components, which will allow them to educate themselves even if they have missed a session. Both intervention modules will be applied in a subsequent order rather than to deliver physiotherapy and psychotherapy at the same time. This approach was chosen so that participants have to make time for a weekly appointment and estimate the effects of each module separately. Nonetheless, some patients might find it tempting to select the intervention module they find more interesting or suitable for their individual situation and skip the other one. In addition, the subsequent order contributes to the prolongation of the overall treatment period. All psychotherapy sessions will be provided as group treatments. Group sessions will be accompanied by a workbook, which requires that participants adhere to specific assignments and may influence their motivation. Nonetheless, the workbook provides support and advice both during the intervention period and after its completion.

Prior studies suggest that physiotherapy is highly valued by patients with CPPS [6, 96] and can empower them to take responsibility for themselves and their coping with pain [97]. During the design of the intervention, the aspect of empowerment and self-management was emphasized, which was a strength of the study. Moreover, instead of adapting a foreign concept such as the Wise–Anderson Protocol [54], a German, already implemented, physiotherapeutic management approach was used. The combination of physiotherapeutic group and individual sessions is not part of the regular health care in ambulatory settings in Germany and might be unexpected for some participants. While they will be in a confidential setting during individual treatments with the physiotherapist, they will have to cope with several other patients being present during performance of exercises. Nevertheless, this group experience can also have a positive effect on the subjects.

We intend to recruit patients from the CPPS outpatient clinic, which has been ongoing since 2012 and serves as the observational cohort in our study design. This cohort is limited in size, and it could be brought into question whether sufficient patients are willing to participate and fulfil eligibility criteria. Their initial assessment at the outpatient clinic might be several months to years prior and their situation with regard, but non-exclusive, to the CPPS might have changed, resulting in non-participation in the study. However, this feasibility study should provide information for further optimization of the treatment approach and power calculation in future RCTs rather than sufficient testing of programme effects. Because of the exploratory nature of the study, no sample calculation was performed, and the selection of controls was based on pragmatic reasons. Nevertheless, to the authors' knowledge, this study is the first to evaluate a combined programme of psychotherapy and physiotherapy for patients with CPPS while acknowledging the multifactorial aetiology and demand for multimodal therapies [1, 17].

Trial status

The study is currently ongoing. Recruitment of patients started in mid-May 2016 and will continue until the targeted sample size is reached. The first two groups, one that started with physiotherapy and the other with psychotherapy, underwent treatment from June to November 2016. The second two groups started in January 2017 and will be treated until June 2017. The next two groups are supposed to start treatment in July 2017.

Additional file

Additional file 1: Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist (DOC 120 kb)

Abbreviations

CBT: Cognitive behavioural therapy; cmRCT: Cohort multiple randomized controlled trial; CPPS: Chronic Pelvic Pain Syndrome; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders IV; EAU: European Association of Urology; GAD-7: Generalized Anxiety Disorder Scale; GAS: Goal Attainment Scaling; NIH-CPSI: Chronic Prostatitis Symptom Index of the National Institute of Health; PCS: Pain Catastrophizing Scale; PDI: Pain Disability Index; PHQ: Patient Health Questionnaire; PMR: Progressive muscle relaxation; PSQ: Perceived Stress Questionnaire; RCT: Randomized controlled trial; SCID: Structured Clinical Interview for DSM-IV Axis I Disorders; SF-12: 12-Item Short-Form Health Survey; SF-MPQ: Short-Form McGill Pain Questionnaire

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Availability of data and materials
The datasets which will be generated during the current study will be available from the corresponding author on reasonable request.

Participants' safety and adverse events
Participants will be covered by the patient insurance of the University Medical Center Hamburg-Eppendorf. Both the psychotherapy and the physiotherapy will be conducted by health professionals trained specifically and knowledgeable in safe application as well as appraisal of the therapy modalities. However, in case of any adverse event, medical care is available at any time through the University Medical Center Hamburg-Eppendorf. All adverse events will be documented and serious adverse events will be reported to the ethics committee within one working day.

Authors' contributions
CAB is responsible for study design, project management, and editing of the manuscript. SGRK is responsible for writing of the manuscript. CD is responsible for critical revision of the manuscript. BR is responsible for study design and critical revision of the manuscript. SG is responsible for writing of the manuscript. DAT is responsible for preliminary work in the design of the psychotherapeutic treatment rationale and patient workbook. GK is responsible for study design, project management, and editing of the manuscript. BL is responsible for study design, project management, supervision of the study, and editing of the manuscript. All authors commented on the draft and approved the final manuscript.

Ethics approval and consent to participate
The study protocol has been conducted according to the Declaration of Helsinki and has been approved by the Ethics Committee of the Medical Association Hamburg, Germany (2 December 2014; reference number PV4801). Patients, who were contacted during recruitment, have given their consent to be contacted in the future during the initial examination at the CPPS outpatient clinic (which has been approved by the Ethics Committee of the Medical Association Hamburg, Germany; 17 August 2012; reference number PV4220). Patients participating in the feasibility study will sign a separate informed consent form that has been approved by the ethics committee. The informed consent in duplicate will be send to the participants by mail.

Consent for publication
Not applicable.

Competing interests
GK declares that she is a co-founder of the Association for Reflective Respiratory Physiotherapy (Verein für Reflektorische Atemtherapie e.V.), which was established in 2000. She has been a freelance lecturer for reflective respiratory physiotherapy for over 15 years. The other authors declare that they have no competing interests.

Publisher's Note

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Physiotherapy and Combined Cognitive-Behavioural Therapy for Patients with Chronic Pelvic Pain Syndrome: Results of a Non-Randomized Controlled Feasibility Trial.

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Abstract

Objective: To explore feasibility in terms of delivering and evaluating a combination of physio- and psychotherapy for patients with chronic pelvic pain syndrome (CPPS).

Design: Prospective non-randomized controlled pilot study.

Setting: Tertiary care facility with a specialized interdisciplinary outpatient clinic for patients with CPPS.

Participants: A total of 311 patients was approached; 60 participated. Thirty-six patients were included in the intervention group (mean age ± SD 48.6 years ± 14.8; 52.8% female) and 24 in the control group (mean age ± SD 50.6 years ± 14.5; 58.3% female). Fourteen participants were lost to follow up.

Interventions: Participants were non-randomly allocated to the intervention group with two consecutive treatment modules (physiotherapy and cognitive behavioural therapy) with a duration of nine weeks each or to the control group (treatment as usual).

Main outcome measures: Feasibility was operationalized in terms of delivering and evaluating the therapeutic combination. Regarding eligibility as the first aspect of feasibility, willingness to participate, drop-out, and satisfaction were assessed; for the second aspect standardized self-report questionnaires measuring health-related quality of life, depression severity, and pain were applied.

Results: Although eligibility and willingness-to-participate rates were low, satisfaction of the participants in the intervention group was high and drop-out rates were low. Results indicated a small and non-significant intervention effect in health-related quality of life and significant effects regarding depression severity and pain.

Conclusions: The combination of physio- and psychotherapy for patients with CPPS seems to be feasible and potentially promising with regard to effect. However, a subsequent fully powered randomized controlled trial is needed.

Trial registration: German Clinical Trials Register (DRKS00009976) and ISRCTN (ISRCTN43221600).

Keywords: chronic pelvic pain syndrome, cognitive behavioural therapy, physiotherapy, interdisciplinary treatment, feasibility study

Article Summary

Strengths and limitations of this study

- A combination of physiotherapy and psychotherapy is recommended for patients with chronic pelvic pain syndrome; this therapeutic combination is being investigated in this non-randomised controlled feasibility study.
- The fact that both women and men are affected by CPPS was taken into account by including both genders in this study.
- This study was designed as a feasibility study, so that statements on acceptance, feasibility and evaluation methodology are possible; however, due to insufficient power, no robust statements on the difference between the groups are viable.
- In addition to the feasibility testing, various patient-relevant outcomes, e.g. quality of life and pain, were evaluated, which will enable sample size estimation for future, fully powered randomised clinical trials.

- Randomisation could not be carried out, thus the comparability of the two groups is limited.

Introduction

Chronic pelvic pain syndrome (CPPS) is a common chronic pain condition with pain perceived in pelvis-related structures and organs without an apparent pathology for at least six months [1]. Worldwide, prevalence rates in the general population range from 4% to 26.6% in women [2, 3] and 2% to 18% in men [4, 5]. Several risk and contributing factors exist [6], but the aetiology of CPPS is still unclear [7].

Several treatment strategies including psychotherapeutic and physiotherapeutic approaches exist, yet for most of these programmes, a distinct benefit was not found [8-11]. The physiotherapeutic approach with the currently best evidence with respect to pain reduction and improvement in quality of life is manual trigger point therapy alone or in combination with active therapy elements [11]. As for psychotherapy, somatocognitive approaches which encourage body awareness and reflection on pain cognitions might be helpful in reducing pain as demonstrated in a randomized-controlled trial [10]. However, existing reviews demonstrated that the successful treatment of CPPS remains challenging and that single treatment strategies often fail to be satisfactory [9]. A combination of physio- and psychotherapy might be a promising approach in reducing symptoms and increasing quality of life [10], so that a multidisciplinary treatment approach is highly recommended [1, 8, 12]. Nonetheless, to the best of our knowledge, no study has tested the combination of physio- and psychotherapy.

Another argument for a combination of treatment modalities is the heterogeneity of symptoms among patients with CPPS. The spectrum includes urogenital, gastroenterological, and/or sexual dysfunction [13]. CPPS is also associated with myofascial [12, 14] and psychopathological symptoms as well as a decreased health-related quality of life [12, 15-20]. Furthermore, there seems to be a linkage between myofascial and psychosocial factors [14]. The aim of this study was to explore the feasibility of combining physio- and psychotherapy in a common therapy approach for female and male patients with CPPS in terms of delivering and evaluating the therapeutic combination.

Material and Methods

Study design

The study was based on the principles of a "cohort multiple randomized controlled trial" (cmRCT) proposed by Relton et al. [21] Participants were recruited from a specialized outpatient clinic for patients with CPPS based at the University Medical Centre Hamburg-Eppendorf. From August 2012 to December 2017, several studies were conducted within the *Interdisciplinary Research Platform Chronic Pelvic Pain Syndrome (CPPS)* [11, 14-20, 22-24]. In the CPPS outpatient clinic, patients underwent multimodal diagnostic algorithm consisting of psychosomatic, physiotherapeutic, urologic, and gynaecologic assessments. Patients signed informed consent, which allowed the contact for this study. The protocol for the study was

published [23] (see Supplementary File S1 for the original study protocol) and the study was registered at the German Clinical Trials Register (DRKS00009976) and at ISRCTN (ISRCTN43221600). Ethical approval for the CPPS outpatient clinic and for the feasibility study was given by the Ethics Committee of the Medical Association Hamburg, Germany (reference numbers PV4220 and PV4801).

Patient and public involvement

Patients or the public were not involved in the design, the reporting, or the dissemination plans of this pilot study due to its explorative nature. Patients were involved in the conduct of the trial by participating in one of the study arms. The intervention group was asked to share their experiences including burden and time expenditure associated with the intervention.

Participants

All potentially eligible patients from the outpatient clinic cohort were contacted. Inclusion criteria included diagnosis of CPPS according to the EAU guidelines [1] and the International Association for the Study of Pain [25], informed consent, age ≥ 18 years, and sufficient German language skills. Exclusion criteria were delusional disorders or substance dependences with the exception of nicotine or painkillers, and acute suicidal tendencies. In addition, patients were not eligible for the intervention group if they had expected absences during the

treatment period for more than four therapy units or received ongoing physiotherapeutic or psychotherapeutic treatment; however, participation in the control group was possible. All participants who fulfilled inclusion criteria and signed informed consent were non-randomly allocated to either intervention- or control-group. The assignment to the intervention group was based on whether the participant would be able to regularly attend the treatment sessions at the University Medical Centre Hamburg-Eppendorf. The targeted overall size for the intervention group was n = 36 and n = 18 for the control group.

Intervention group

A combination of consecutive cognitive behavioural therapy (CBT) and physiotherapy was used in the intervention group. Both therapy modalities were applied in sex homogenous groups in separate modules with a four-week break between each module. The physiotherapy module was a combination of three 90-minutes group sessions and six individually scheduled treatment sessions, each lasting 60 minutes for nine weeks. Following the German physiotherapeutic concept of reflective respiratory physiotherapy (Reflektorische Atemtherapie®) [26], the single sessions included heat applications, manual techniques, specific therapeutic movements, and educational parts, whereas group sessions focused on active exercises, self-management strategies, and education. The psychotherapeutic intervention incorporated nine weekly 90-minutes group sessions CBT including theory parts, group discussions, and Progressive Muscle Relaxation (PMR) [27]. Key topics for the cognitive behavioural intervention were behaviour analysis, positive self-messages, reduction of fear-avoidance-beliefs and behaviour, improvement of physical

activity, development of coping strategies, management of catastrophizing cognitions, and enhancement of social support. A supplementary work book based on the work of Tripp et al. [28] was developed. Participants who had accumulated more than six sessions dropped out of the intervention group.

Control group

The control group received treatment as usual. The patients were allowed to participate in standard medical care as performed in Germany. This includes, for example, outpatient treatment by a general practitioner or specialist. Hence, they did not receive any specific treatment within this study.

Assessments

Measurements of all participants were taken at the time of the visit of the outpatient clinic (t1), during the recruitment process at baseline (t2), and at the end of the second intervention module (t6). The intervention group was assessed additionally at the beginning (t3) and the end of the first intervention module (t4), at the beginning of the second module (t5), and four weeks after the end of the second module (t7).

Feasibility of delivering the combined intervention was operationalized in terms of willingness-to-participate, reasons for refusing to participate and attendance rate. In

addition, the acceptance of this therapeutic intervention by the patients was operationalized by a questionnaire assessing the satisfaction of the participants. This questionnaire was designed specifically for this study and contained Likert scales as well as open questions, which gave participants the opportunity to share their thoughts on this combined intervention.

A major concern of this feasibility study was also to provide effect sizes for power calculations for randomized clinical trials to be planned in the future. For this purpose, the effect sizes for different self-report scales were calculated. A power calculation for the present study was consequently not performed, also due to the nature of a feasibility study. The conduct of the inferential statistical analyses, including the determination of effect sizes, also served to analyze the feasibility of the analysis methods for future studies. When interpreting statistical significance in the context of this study, the small sample size, the insufficient power and the non-randomized design must be taken into account. Thus, the main psychometric outcome for the feasibility of the evaluation, the health-related quality of life, was measured with the 12-Item Short-Form Health Survey (SF-12) [29]. Additionally, somatic symptom severity, anxiety severity, and depression severity were assessed with the German version [30] of the Perceived Stress Questionnaire (PSQ) [31], the Patient Health Questionnaire PHQ-15 [32], the Generalized Anxiety Disorder Scale (GAD-7) [33], and the Patient Health Questionnaire PHQ-9 [34] respectively. The German version [35] of the Chronic Prostatitis Symptom Index of the National Institute of Health (NIH-CPSI) [36] and an adapted version for women with CPPS [37] were used to measure the symptom burden. Pain in conjunction with disability, perception, and catastrophizing were measured using the German version [38] of the Pain Disability Index (PDI) [39], the German version [40] of the Pain Catastrophizing Scale (PCS) [41], and the German version [42] of the Short-Form McGill Pain Questionnaire (SF-MPQ) [43]. In the

physiotherapeutic examination of the intervention group, performed at the time points t3, t5, and t7, tender and trigger points in predefined muscles were manually palpated.

Two adaptations in the outcome measures had to be made after registration: Originally, it was planned to use attainment of individual patient goals in the intervention group measured with the goal attainment scale after each module and four weeks after overall treatment. However, the patients were not used to goal setting and the assessment of their goals resulted in feelings of discomfort and insecurity. Hence, goal attainment was dropped as an outcome. The other previously planned outcome, selective attention on pain-related stimuli as measured by a computer-based dot-probe-task, was also dropped due to technical difficulties, which arose during the study process.

Statistical Analysis

Chi-square tests respectively Fisher's exact tests and t-tests for independent groups were calculated for baseline comparisons. Regarding feasibility with emphasis on acceptance, the eligibility rate, the willingness-to-participate rate, and the dropout rate were calculated. Additionally, the most frequent reasons for not being eligible, not willing to participate, and for dropping-out were presented. Moreover, we compared whether absence differed between modules and whether the overall treatment satisfaction differed from each module by conducting repeated measure analyses of variance (ANOVA).

Prior to the efficacy estimation analysis, which was done in order to gain insight into feasibility of evaluation, missing values in the self-report instruments were imputed using the expectation-maximization (EM) estimation method [44], provided that completion rate of a questionnaire for a particular participant at a particular time point was at least 60%. To establish consistency of efficacy estimations, all analyses were adjusted for baseline and sex as well as the interaction between sex and group affiliation at t2 and t6. The primary efficacy estimations were defined as the differences between intervention and control group after the treatment (t6) using analyses of covariance (ANCOVA) with adjustments for the respective baseline values at t2. Furthermore, potential sequence effects within the intervention group (psychotherapy followed by physiotherapy vs physiotherapy followed by psychotherapy) were analysed by comparing the outcomes at the end of the treatment (t6). In addition, sex effects were interpreted comparing the intervention and the control group at the end of the treatment.

Due to the exploratory nature of this study, corrections for multiple testing were not applied. For all efficacy estimations as well as comparisons of the absence and the treatment satisfaction rates, Cohen's d was calculated as an indicator of effect size. The effect sizes were classified as small ($d \geq 0.2$), medium ($d \geq 0.5$), or large ($d \geq 0.8$) [45]. Two-tailed p-values <0.05 were considered significant. All statistical analyses were conducted with IBM SPSS 24. In addition to the quantitative analyses, the trajectories for measurements of quality of life and CPPS symptoms were presented in line graphs. Furthermore, anecdotal quotes from the free text fields in the questionnaires in German were translated and used to illustrate the range of feedback.

Results

From October 2012 to June 2017, 311 persons visited the specialized outpatient clinic. Of these, 103 patients did not meet the inclusion criteria or displayed no interest in study participation at the initial screening; thus, 208 patients were further assessed for eligibility. Of these, an additional 148 patients were excluded due to failure to meet the inclusion criteria or other reasons, with 36 participants remaining in the intervention group and 24 participants remaining in the control group (Figure 1). Table 1 illustrates the demographic and psychometric characteristics of the participants. No significant differences between the groups were found.

Feasibility of delivering and satisfaction

The eligibility rate, when considering all screened persons (n = 311), was 44.7%. The main reasons for ineligibility was absence of a CPPS diagnosis and unattainability of patients. Of all eligible persons (n = 172), sixty consented to take part in the study; resulting in a willingness-to-participate rate of 34.8%. Patients who were eligible but rejected participation indicated mostly to have no interest or no time. Of the 36 persons in the intervention group, one participant dropped out prior to the first therapy unit and nine participants dropped out during the intervention period -resulting in a dropout rate of 27.8%. The adjusted average proportion of missed sessions was M = 36.33 % (SE = 4.93) for the psychotherapeutic

module, and M = 30.03 % (SE = 6.24) for the physiotherapeutic module revealing no significant differences.

In general, patients gave high ratings of treatment satisfaction (Table 2). The following quotes from the satisfaction questionnaires were selected to illustrate the breadth of patient feedback:

> *"The CPPS study has helped me managing the daily life with my pain and […] I can get better through the day. Talking about perception of the pain and its treatment […] has positively affected me."*

> *"The manual, the group, and the conversations were helpful. But I still had the need to talk and in the group, I was not confident enough to talk about everything (I would have liked to.)."*

> *"The interaction with other affected people (patients) was helpful. The contents are easy/good to take into practice. The duration of the group therapy was, in my opinion, too short. The double number of appointments would be appropriate for the input."*

Feasibility of evaluation and estimation of efficacy

As indicated by the main efficacy estimations, which serve as indicators for feasibility of evaluation, no significant differences or medium effect sizes were found for the SF-12 at the end of the intervention (Table 3). With respect to the secondary outcomes, the intervention

group reported significantly lower symptom burden as measured by the PDI (p = 0.02, d = -0.73), and the PHQ-9 (p = 0.04, d = -0.62). Table 4 displays the results of the analysis of sex-related effects. Neither main effects for sex nor sex*group interaction effects were significant.

Regarding the analysis of sequence effects within the intervention group, no significant differences were found in the SF-12. With respect to the secondary outcomes, the sequence psychotherapy-physiotherapy was significantly superior to the sequence physiotherapy – psychotherapy in pain reduction as measured by the NIH-CPSI pain subscale (p = 0.03, d = -1.12).

Figure 2 displays the courses of the most important outcome variables across all times of measurement. Besides the aforementioned results, the figure suggests reductions in the Physical and Mental Component Summaries of the SF-12 and increases in the PDI, the NIH-CPSI, the PHQ-9 and the PCS between t6 and follow-up in the intervention group.

Discussion and conclusions

This study explored feasibility of a combined psycho- and physiotherapy in patients with CPPS in terms of delivering and evaluating. Although several challenges arose during recruitment, the intended sample size could be reached and participants expressed high satisfaction with the treatment. Furthermore, we received some insights on possible

treatment effects in comparison with the treatment-as-usual group. Specifically, we found significant lower symptom burden in the intervention group as measured with the PDI and the PHQ-9 but no significant changes in the SF-12. Our results showed that delivering a combination of psycho- and physiotherapy was feasible; however, based on experiences in this study, some adaptations when conducting this programme in the future seem necessary. The evaluation of this intervention also demonstrated to be feasible using analysis of covariances; however, some instruments seemed to be more suitable in demonstrating effects than others.

Compared to the literature [46], the eligibility rate and the willingness-to-participate rate were lower than the median rates in other clinical trials. One of the main reasons of the low eligibility was the circumstance that patients could refer themselves to the specialized outpatient clinic. Thus, many patients did not have a CPPS diagnosis or were only interested in the diagnostic algorithm but not in the treatment study. Moreover, the low eligibility rate might be attributed to the time lag between initial eligibility screening and trial inclusion. In our study, up to 3 ½ years have passed since the patient's last appointment at the outpatient clinic and the inquiry for the study. Since it was a rather long time, several factors might have affected eligibility: First, many patients were unattainable due to re-locations or other, mostly unknown, reasons. Second, given the natural course of chronic pain, nearly one third of the patients have less symptoms over time or are even symptom-free [47]. Third, patients with CPPS were likely to use other health care services in order to find pain relief [48]. Future trials should strive for a shorter time period between first contact with the patient and trial inclusion. Nevertheless, although the recruitment process faced these challenges, the

intended sample size could be reached underlining the feasibility of the study. The feasibility of the physio- and psychotherapy combination treatment was also supported by the low dropout rates for the intervention in total and for psycho- and physiotherapy separately. These rates were smaller in comparison to the literature [49, 50] and indicated high acceptance of the treatment. Finally, the feasibility is also indicated by the high level of satisfaction expressed by the participants. Satisfaction with the treatment is suggested to be a basic component for carrying out a successful psychotherapeutic and physiotherapeutic treatment [51]. However, directly comparing this study with existing studies is difficult, since, to the best of our knowledge, this is the first study to investigate combined physio- and psychotherapy in patients with CPPS.

While the eligibility rate was still within the interquartile range of examined studies by Gross et al. [46], the willingness-to-participate rate was considerably below the interquartile range. Although the majority of persons perceived research to be very important, the willingness to participate often depends on convenience and whether or not study participation interfered with the daily routine [52]. Moreover, patients are more likely take part in a study if the home-study site distance is short [53]. In our study, perceived lack of time, long distance to study site, and/or no interest were the most common reasons to refuse participation. Our willingness to participate rate would have improved substantial if we had delivered as least some parts of the intervention in a flexible, possible online format. Hence, these barriers should be targeted when designing future studies. One possible solution might be to concept at least some of the treatment sessions as online sessions. Not only do online programmes enable treatments independent of the home-study site distance, but also allow participants to

better integrate the content of the therapy into their daily routine [54]. Furthermore, online programmes provide continuity of care during pandemic situations like the COVID-19 outbreak [55].Taking these adaptations in mind, we deem our combined intervention feasible and accepted by the patients.

Besides delivering feasibility, we also looked at effect sizes in order to explore evaluating feasibility. Several psychometric indicators showed that the intervention group improved in comparison to the control group although only the estimation of effect size measured with the PDI and the PHQ-9 reached significance level. Nevertheless, the intervention seems to be more effective than treatment as usual in terms of reduction of pain disabilities and depressive symptoms. Interestingly, the sequence psychotherapy first, physiotherapy second appears to be more effective than the other way around. Similar findings were observed in patients with chronic neck pain, who had greater effects in pain and disability reduction as well as quality of life when combining psychotherapy with subsequent physiotherapy. The authors conclude, that patients would need the physical performance in which they can apply and train the theoretical content of the cognitive behavioural therapy [56]. We have found that the intervention effects did not differ by gender. One possible explanation could be that women and men with CPPS have similar symptom patterns. Previous studies have shown that both sexes had similar pain intensity levels [57] and that the proportion of mental disorders is elevated in comparison to the general population in both women and men [16]. Hence, with the assumption of symptoms akin, the intervention might have had worked similar for female and male patients with CPPS. Nevertheless, the sex-disaggregated subsamples were small, which might affect the effect sizes [58].

Prior to conducting an RCT, it is important to perform a power calculation to estimate the optimum sample size. For this purpose, the given effect sizes can be used. The Covid-19 pandemic also shows that online formats can be helpful to avoid treatment interruptions and to reach patients from rural areas more easily. An important point is that in addition to the professional groups involved, the patients' perspective should be included in the study design. While this feasibility study focused on acceptance, the next step should be to investigate the efficacy of the treatment with an appropriate design. Future studies should emphasize possible sex differences in order to tailor the interventions more specifically and effectively to the respective target group. To increase generalizability, a multi-centre study would be the best option.

Limitations

Some limitations of the study should be mentioned. The SF-12 showed only a small and non-significant effect. The failure to detect a significant effect might be attributed to the small sample size of the study, but it could also be due to the generic nature of the instrument, which is not precise enough to detect changes in quality of life in patients with CPPS. This phenomenon was observed in patients with chronic low back pain [59] and thus might also be true for patients with CPPS. Usage of a CPPS-specific instrument like the NIH-CPSI [36] instead of generic outcomes might be considered in future trials. Furthermore, this study is a

feasibility study, which included a small, non-sufficient sample for testing the feasibility of the evaluation and for efficacy testing. Due to the small sample, we rather focused on the effect size Cohen's d than on the statistical significance. Although the effect size is more robust in small samples than the p-value, it is not completely unaffected by sample size [58]. Owing to the construction of the study as a monocentric pilot study, allocation to intervention and control group was non-randomized, which might cause variations in the distribution of sample characteristics. However, no significant differences in study characteristics could be detected between the two branches, which does not give support for the presence of bias. Thus, at this stage of research a non-randomized feasibility study seemed reasonable. It provides first hints that a combined physio- and psychotherapy treatment might be beneficial and that the evaluation of the effect using psychometric questionnaires focussing on pain disabilities rather than quality of life is feasible. However, some studies, which administered either physio- or psychotherapy, exist. The German concept reflective respiratory physiotherapy as such has not been tested, but the American Wise-Anderson-Protocol includes similar therapeutic elements. A case series with male patients demonstrated decreased pain intensity and improved quality of life [60]. The psychotherapeutic programme applied in this study was tested with a group of Canadian men showing positive effects in terms of pain intensity, catastrophizing and quality of life [61]. In comparison, the combination of both therapeutic approaches in this study also indicate, amongst other positive effects, that pain and catastrophizing decreased, and quality of life increased. Nonetheless, since existing studies are highly heterogeneous, comparing this study with available literature should be viewed with caution. Furthermore, the absence of a patient perspective in the design of the study may also have an impact on the acceptance of the therapy.

Finally, we would like to state that this study provides valuable insights for further randomized, multicentre studies; not only regarding the acceptance and the effect of the intervention, but also regarding the recruitment process. The first results of a combined physio- and psychotherapeutic treatment for patients with CPPS appear to be promising although some adaptations to the treatment programme had to be made as outlined above. Further testing of this procedure is therefore urgently needed to provide adequate and scientifically based treatment for patients with CPPS.

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Competing Interests

Gesche Ketels declares that she is a co-founder of the Association for Reflective Respiratory Physiotherapy (Verein für Reflektorische Atemtherapie e.V.), which was established in 2000. She has been a freelance lecturer for reflective respiratory physiotherapy for over 15 years. The other authors declare that they have no competing interests.

Author Contributions

Christian. A. Brünahl: Conceptualization, Writing – Review & Editing, Supervision, Project administration, Funding acquisition; ***Susanne G.R. Klotz:*** Investigation, Data Curation, Writing – Original Draft, Visualization; ***Christoph Dybowski:*** Formal analysis, Investigation, Data Curation, Writing – Review & Editing, Visualization; ***Rebecca Albrecht:*** Investigation, Writing – Review & Editing; ***Johanna Höink:*** Resources, Writing – Review & Editing; ***Margit Fisch:*** Resources, Writing – Review & Editing; ***Gesche Ketels:*** Conceptualization, Writing – Review & Editing, Funding acquisition; ***Bernd Löwe:*** Conceptualization, Resources, Writing – Review & Editing, Supervision, Funding acquisition.

Data Sharing Statement

Technical appendix, statistical code, and dataset available upon reasonable request from the corresponding author.

Ethics Statement

This study (reference number PV4801) and the CPPS outpatient clinic, from which the participants were recruited (reference number PV4220), were approved by the Ethics Committee of the Medical Association Hamburg, Germany.

Supplemental Material

S1: Original study protocol in German handed in to the ethics committee

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Table 1: Comparison of demographic and clinical characteristics at baseline

Variable	Intervention group (n = 36)	Control group (n = 24)	p-value
Demographic characteristics			
Female, % (n)	52.8 (19)	58.3 (14)	.67*
Age in years, mean (SD)	48.6 (±14.8)	50.6 (±14.5)	.60‡
Marital status, % (n)•	(n = 35)	(n = 22)	.29†
Single	37.1 (13)	27.3 (6)	
Married	37.1 (13)	45.5 (10)	
Divorced	25.7 (9)	18.2 (4)	
Other	0	9.1 (2)	
Educational level, % (n)•	(n = 28)	(n = 20)	.13†
6 years of secondary school	14.3 (4)	20.0 (4)	
8 years of secondary school	28.6 (8)	55.0 (11)	
High school graduation	53.6 (15)	25.0 (5)	
Other	3.6 (1)	0	
Pain duration in years, mean (SD)	6.2 (4.8)	6.2 (4.8)	.98‡
Psychometric assessments, mean (SD)			
GAD-7	7.9 (5.5)	6.5 (5.1)	.33‡
PCS	23.4 (13.6)	22.9 (16.1)	.90‡
PDI	26.7 (15.2)	26.6 (18.3)	.95‡
PHQ-9	9.9 (5.8)	9.1 (6.9)	.65‡
PHQ-15	11.0 (5.0)	10.3 (6.0)	.63‡
PSQ	0.5 (0.2)	0.5 (0.2)	.78‡
SF-12 PCS	39.5 (8.5)	38.0 (12.0)	.61‡
SF-12 MCS	39.9 (11.9)	40.2 (11.1)	.93‡
SF-MPQ total	18.2 (9.4)	18.6 (12.5)	.89‡
SF-MPQ sen.	13.2 (7.1)	14.6 (8.6)	.52‡
SF-MPQ aff.	5.0 (3.2)	4.0 (4.2)	.33‡
NIH-CPSI total	24.1 (7.4)	23.7 (7.6)	.83‡
Pain subscale	11.3 (3.8)	11.4 (3.7)	.92‡
Urinary subscale	4.7 (2.9)	4.1 (2.7)	.38‡
QoL subscale	8.0 (2.3)	8.2 (2.7)	.85‡

Legend: •assessed at outpatient clinic visit (t1); *Chi²; ‡t-test for independent samples; †Fisher's exact test; GAD-7 = Generalized Anxiety Disorder Screener; NIH-CPSI = Chronic Prostatitis Symptom Index of the National Institutes of Health; PCS = Pain Catastrophizing Scale; PDI = Pain Disability Index; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); PHQ-15 = Patient Health Questionnaire 15 (somatic symptoms); PSQ = Perceived Stress Questionnaire; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ aff. = affective subscale of Short Form McGill Pain Questionnaire; SF-MPQ sen. = sensory subscale of Short Form McGill Pain Questionnaire; SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; SD = standard deviation

Table 2: Treatment satisfaction

	All		Female		Male		Overall comparisons		
							Modules[a]	Sex	Modules*sex
	N	Est. M (SE)	N	Est. M (SE)	N	Est. M (SE)	p (d)	p (d)	p (d)
Overall treatment	25	6.0 (0.2)	14	5.9 (0.3)	11	6.2 (0.3)	0.08 (0.72)	0.37 (0.38)	0.89 (0.10)
Psychotherapeutic module	25	5.4 (0.3)	14	5.1 (0.4)	11	5.6 (0.4)			
Physiotherapeutic module	25	5.9 (0.3)	14	5.6 (0.4)	11	6.1 (0.5)			

Legend
Items: "Would you recommend …?"; scale from 1 = „does not apply at all" to 7 = "fully applies";
higher values correspond with higher treatment satisfaction.
Est. M = estimated mean; SE = standard error
[a]Overall treatment vs psychotherapeutic module vs physiotherapeutic module

Table 3: Post-treatment (t6) comparisons between the intervention group and the control group, adjusted for baseline (t2), sex, and the interaction of sex*group

	Intervention group			Control group			Comparison					
Outcome variable	n	Est. mean	SE	n	Est. mean	SE	Mean difference	ES	ES SE	ES CI 95% lower limit	ES CI 95% upper limit	p
SF-12 PCS	22	44.2	1.3	23	41.7	1.3	2.5	0.40	0.3	-0.19	0.99	0.18
SF-12 MCS	22	42.8	1.9	23	41.4	1.9	1.4	0.15	0.3	-0.43	0.74	0.61
PDI	22	18.4	2.3	22	26.5	2.4	-8.1	**-0.73**	0.3	-1.34	-0.12	**0.02**
NIH-CPSI total	22	18.6	1.5	23	20.8	1.5	-2.2	-0.31	0.3	-0.90	0.28	0.30
Pain subscale	22	8.6	0.8	23	9.5	0.8	-0.8	-0.22	0.3	-0.81	0.37	0.46
Urinary subscale	22	3.7	0.4	23	3.8	0.4	-0.1	-0.04	0.3	-0.63	0.54	0.88
QoL subscale	22	6.4	0.5	23	7.5	0.5	-1.2	-0.50	0.3	-1.10	0.09	0.10
SF-MPQ total	22	12.3	1.7	22	15.6	1.7	-3.2	-0.40	0.3	-1.00	0.20	0.19
SF-MPQ sensory	22	9.7	1.2	22	11.2	1.2	-1.5	-0.27	0.3	-0.86	0.33	0.38
SF-MPQ affective	22	2.7	0.6	22	4.2	0.6	-1.5	-0.55	0.3	-1.16	0.05	0.08
PCS	22	14.7	1.8	22	19.5	1.8	-4.8	-0.56	0.3	-1.17	0.04	0.07
PHQ-9	22	6.9	0.9	22	9.5	0.9	-2.6	**-0.62**	0.3	-1.23	-0.02	**0.04**
GAD-7	22	5.7	0.9	22	6.5	0.9	-0.9	-0.21	0.3	-0.81	0.38	0.48
PHQ-15	22	9.9	0.8	21	9.8	0.8	0.2	0.04	0.3	-0.56	0.64	0.89
PSQ	22	0.4	0.0	22	0.5	0.0	-0.0	-0.14	0.3	-0.74	0.45	0.64

Legend

p-values <.05 and corresponding ES are presented in bold
Est. = estimated; SE = standard error; ES = effect size Cohens' d; ES
SE= standard error of the effect size;
ES CI = confidence interval of the effect size
SF-12 PCS = 12-Item Short Form

Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ sensory = sensory subscale of the Short Form McGill Pain Questionnaire; SF-MPQ affective = affective subscale of the Short Form McGill Pain Questionnaire; PCS = Pain Catastrophizing Scale; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); GAD-7 = Patient Health Questionnaire Generalized Anxiety Disorder Screener; PHQ-15 = Patient Health Questionnaire 15 (severity of somatic symptoms); PSQ = Perceived Stress Questionnaire

Table 4: Sex-dependent post-treatment (t6) comparisons between the intervention group and the control group

	Female patients								Male patients										
	Intervention group			Control group			Comparison		Intervention group			Control group			Comparison		Overall		
Outcome variable	n	Est. mean	SE	n	Est. mean	SE	Mean diff.	ES	n	Est. mean	SE	n	Est. mean	SE	Mean diff.	ES	ES diff.	p main effect sex	p interaction sex*group
SF-12 PCS	10	45.6	1.9	14	43.0	1.6	2.6	0.44	12	42.7	1.7	9	40.4	2.0	2.3	0.39	0.05	0.13	0.94
SF-12 MCS	10	41.0	2.9	14	39.9	2.4	1.1	0.12	12	44.6	2.6	9	42.8	3.0	1.8	0.20	-0.08	0.24	0.90
PDI	10	18.8	3.5	13	26.4	3.0	-7.6	-0.69	12	18.0	3.2	9	26.6	3.7	-8.6	-0.79	0.09	0.92	0.88
NIH-CPSI total	10	19.5	2.2	14	19.9	1.9	-0.4	-0.05	12	17.7	2.0	9	21.8	2.3	-4.1	-0.59	0.53	0.97	0.38
Pain subscale	10	8.9	1.2	14	8.9	1.0	0.0	0.01	12	8.3	1.1	9	10.0	1.2	-1.7	-0.46	0.47	0.78	0.44
Urinary subscale	10	4.3	0.7	14	3.9	0.6	0.4	0.20	12	3.0	0.6	9	3.7	0.7	-0.6	-0.29	0.50	0.23	0.41
QoL subscale	10	6.4	0.7	14	7.1	0.6	-0.8	-0.34	12	6.3	0.7	9	7.9	0.8	-1.6	-0.68	0.34	0.61	0.58
SF-MPQ total	10	12.5	2.5	13	15.6	2.2	-3.1	-0.39	12	12.2	2.3	9	15.6	2.6	-3.4	-0.43	0.04	0.93	0.94
SF-MPQ sensory	10	10.4	1.8	13	11.3	1.6	-1.0	-0.17	12	9.1	1.6	9	11.2	1.9	-2.1	-0.37	0.20	0.66	0.74
SF-MPQ affective	10	2.4	0.9	13	4.2	0.7	-1.8	-0.67	12	3.0	0.8	9	4.3	0.9	-1.3	-0.47	-0.20	0.66	0.75
PCS	10	12.6	2.7	13	19.7	2.3	-7.2	-0.86	12	16.8	2.4	9	19.2	2.8	-2.4	-0.29	-0.57	0.48	0.37
PHQ-9	10	6.9	1.3	13	10.0	1.1	-3.1	-0.75	12	6.9	1.2	9	9.0	1.4	-2.1	-0.52	-0.23	0.70	0.70
GAD-7	10	5.5	1.3	13	5.5	1.1	0.0	0.00	12	5.8	1.1	9	7.5	1.3	-1.7	-0.43	0.43	0.38	0.48
PHQ-15	10	10.3	1.1	12	9.7	1.0	0.6	0.18	12	9.5	1.0	9	9.8	1.2	-0.3	-0.09	0.27	0.74	0.67
PSQ	10	0.4	0.0	13	0.5	0.0	0.0	-0.29	12	0.5	0.0	9	0.5	0.0	0.0	0.00	-0.29	0.80	0.64

Legend:
SE = standard error; Est. = estimated; diff. = difference; ES = effect size Cohen's d
SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QoL = Quality of Life; SF-MPQ =Short Form McGill Pain Questionnaire; SF-MPQ sensory = sensory subscale of the Short Form McGill Pain Questionnaire; SF-MPQ affective = affective subscale of the Short Form McGill Pain Questionnaire; PCS = Pain Catastrophizing Scale; PHQ-9 = Patient Health Questionnaire 9 (depressive symptoms); GAD-7 = Patient Health Questionnaire Generalized Anxiety Disorder Screener; PHQ-15 = Patient Health Questionnaire 15 (severity of somatic symptoms); PSQ = Perceived Stress Questionnaire

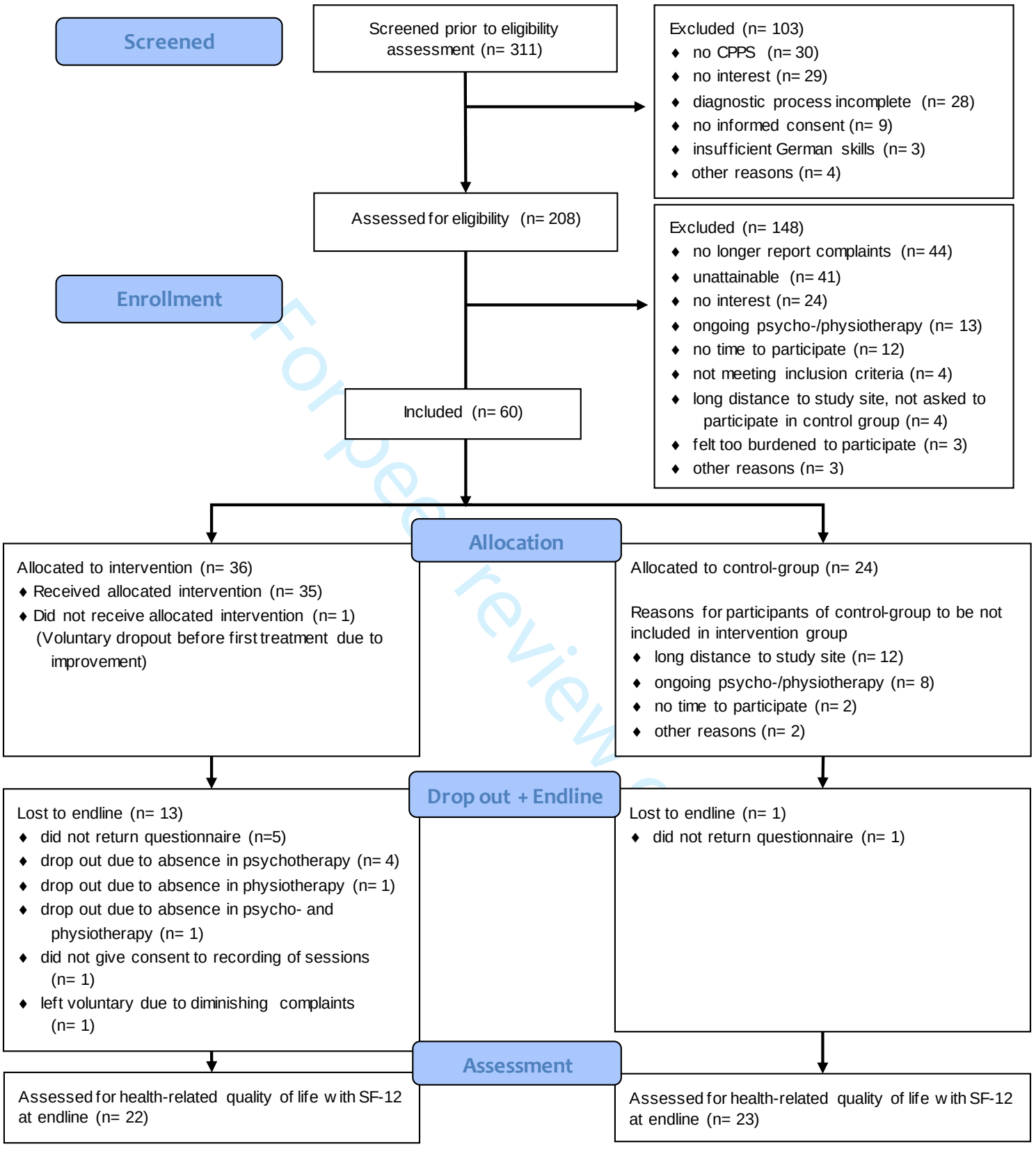
Figure 1: Flow of participants

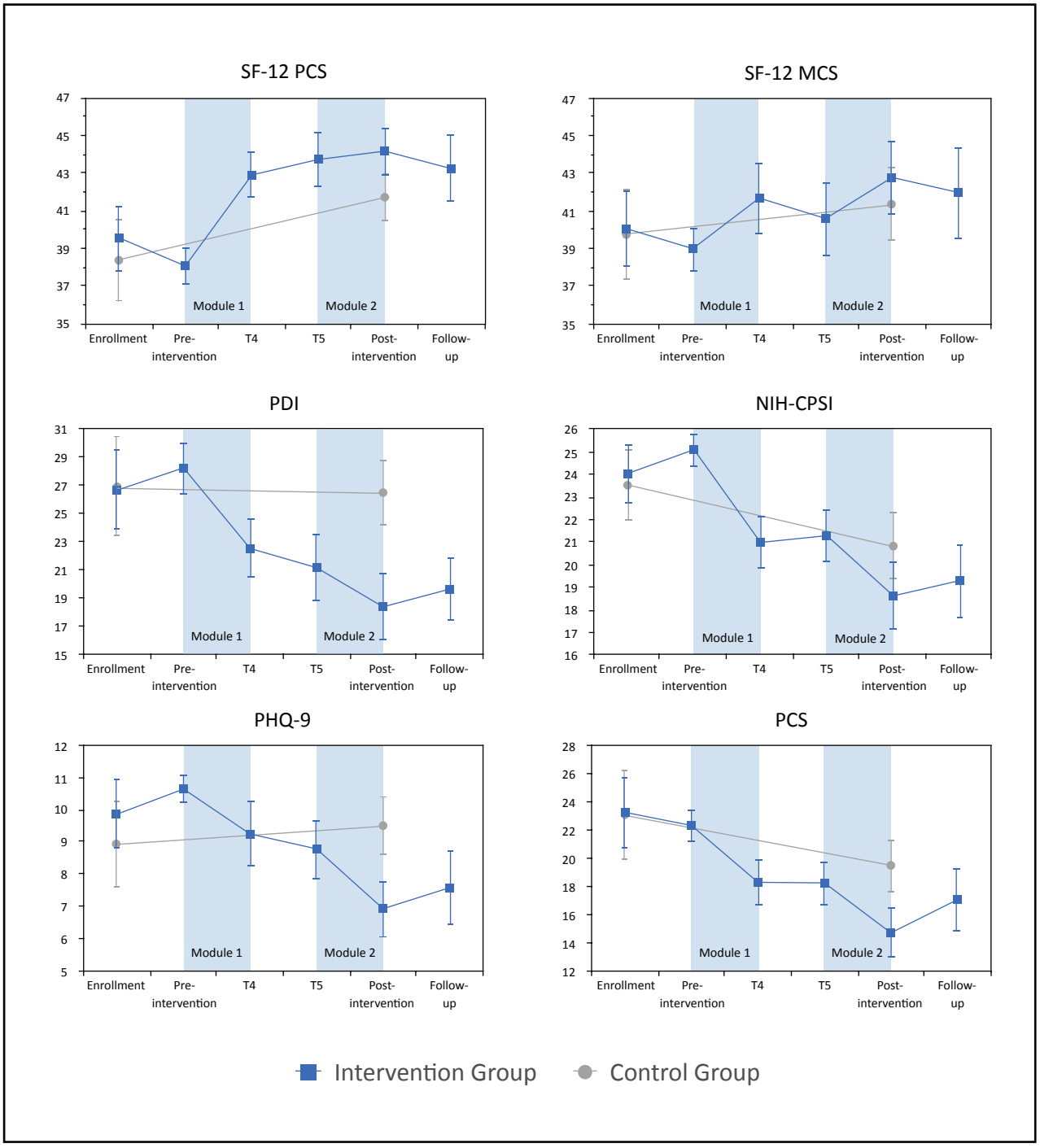
Legend: SF-12: 12-Item Short Form Health Survey

Source: Eldridge et al. (2016)

Figure 2: Course of important outcome variables in the intervention and the control group

Legend: SF-12 PCS = 12-Item Short Form Health Survey Physical Component Summary; SF-12 MCS = 12-Item Short Form Health Survey Mental Component Summary; PDI = Pain Disability Index; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; PHQ-9 = Patient Health Questionnaire 9; PCS = Pain Catastrophizing Scale




SF-12 PCS
SF-12 MCS
PDI
NIH-CPSI
PHQ-9
PCS
Module 1
Module 2
Enrollment
Pre-intervention
T4
T5
Post-intervention
Follow-up
Intervention Group
Control Group

STUDIENPROTOKOLL

Pilotstudie zur Machbarkeit und Wirksamkeit eines kombinierten kognitiv-verhaltenstherapeutischen und physiotherapeutischen Behandlungsprogramms für Patientinnen und Patienten mit chronischem Unterbauchschmersyndrom im Rahmen der Interdisziplinäre Forschungsplattform „Chronic Pelvic Pain Syndrome (CPPS)“

Hamburg, 10. Juli 2014

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1.4 Voraussichtliche Studiendauer

5 Jahre; 1. September 2012 – 31. August 2017

1.5 Zusammenfassung

Das Krankheitsbild des „Chronic Pelvic Pain Syndrome (CPPS)“ betrifft beide Geschlechter gleichermaßen mit bedeutsamen Prävalenzraten.

Es existieren aktuell weder ein gesichertes Wissen über die Entstehungs- und Aufrechterhaltungsmechanismen des CPPS, noch effektive Behandlungsformen. Insbesondere die Beteiligung psychischer Faktoren sowie das Bestehen psychischer Komorbidität wurden in der wissenschaftlichen Literatur erst in den vergangenen Jahren mehr betrachtet.

Es existiert eine diagnostisches Modell, das die Beschwerden des Patienten auf mehreren somatischen Ebenen erfasst, aber auch eine psychologische und eine physiotherapeutische Diagnostik verlangt. Entsprechend der diagnostischen Einschätzung über die einzelnen Ebenen wird dann eine Behandlungsempfehlung gegeben. Es existieren bisher ein psychotherapeutischer und ein physiotherapeutischer Ansatz. Beide Behandlungsmodelle wurden bislang ausschließlich bei männlichen Patienten angewendet und befinden sich im Stadium der Pilotstudien. Zudem wurden die einzelnen Behandlungsoptionen in der Vergangenheit stets isoliert, nicht aber in einer strukturierten Kombination angewendet. Die vorliegende Pilotstudie soll dies leisten: Es wird eine Kombinationsbehandlung mit einem psychotherapeutischen und einem physiotherapeutischen Modul für beide Geschlechter angeboten. Es handelt sich um den ersten Ansatz im deutschsprachigen Raum, so dass auch die Frage der Machbarkeit geklärt werden soll.

Den Hintergrund für die Therapiestudie bildet die interdisziplinäre Forschungsplattform „Chronic Pelvic Pain Syndrome (CPPS)“ am Universitätsklinikum Hamburg-Eppendorf. Hierüber werden die Patientinnen und Patienten rekrutiert.

Die Pilotstudie zur verhaltenstherapeutischen und physiotherapeutischen Kombinationsbehandlung hat zum Ziel, je zwei Gruppen mit 6 Teilnehmerinnen / Teilnehmern geschlechtshomogen und zwei Gruppen geschlechtsheterogen. Damit wird eine Gesamtstichprobengröße von n = 36 erzielt. Primärer Endpunkt ist die gesundheitsbezogene Lebensqualität (SF-12). Daneben werden körperliche Symptommaße, psychologische Variablen (z.B. Katastrophisierende Kognitionen) und Patientenzentrierte Aspekte (z.B. Patientenzufriedenheit) erhoben.

2. Stand der Forschung und eigene Vorarbeiten

2.1 Darstellung des bisherigen Wissensstandes

2.1.1 Stand der Forschung

Verbreitung und Diagnostik

Das chronische Unterbauchschmerzsyndrom bezeichnet ein mindestens sechs Monate anhaltendes Beschwerdebild, das z.B. beim Mann Symptome einer Prostatitis oder Beschwerden in angrenzenden Strukturen aufweisen kann, ohne jedoch durch einen somatischen Befund ausreichend erklärt zu werden. Das Leitsymptom ist der Schmerz im Beckenboden- und Genitalbereich.[1] Ferner klagen Betroffene über Blasenentleerungsstörungen, sexuelle Dysfunktionen und Erschöpfungszustände. Aufgrund des Fehlens einer erklärenden somatischen Beteiligung wird das chronische Unterbauchschmerzsyndrom beim Mann auch als abakterielle Prostatitis bezeichnet. Das Krankheitsbild der Prostatitis wird in einem Klassifikationssystem differenziert, das seit der Veröffentlichung 1995 durch das National Institute of Diabetes and Digestive and Kidney Diseases weltweit verwendet wird.[2] Es werden vier Typen unterschieden:

- I Akute bakterielle Prostatitis
- II Chronische bakterielle Prostatitis
- III Chronische abakterielle Prostatitis
  - A mit nachweislicher Entzündung
  - B ohne nachweisliche Entzündung
- IV Asymptomatische entzündliche Prostatitis

Bei vorliegender abakterieller Prostatitis (Typ III) dient der National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) zur Erfassung der Schwere der Symptomatik sowie des Einflusses auf die Lebensqualität der Patienten.[3] Dieser Fragebogen liegt auch in einer weiblichen Form (englische Fassung) vor.[4] Die männliche Version des NIH-CPSI steht in einer deutschsprachigen, validierten Fassung zur Verfügung.[5]

Die Leitlinien der European Association of Urology (EAU)[6] definieren den Chronischen Beckenschmerz (Chronic Pelvic Pain, CPP) als anhaltenden Schmerz bei Männern und Frauen, der in Körperbereichen erlebt wird, die mit dem Becken in Zusammenhang stehen. Die Symptomatik muss dabei mindestens 6 Monaten anhalten, wobei auch zyklische Verläufe möglich sind. Ferner sind prädisponierende Faktoren, viszerale und muskuloskelale Dysfunktionen, emotionale Folgen, Auswirkungen auf das Verhalten sowie sexuelle und soziale Konsequenzen zu beachten.[7] Die Leitlinien der EAU differenzieren CPP mit Hilfe eines axialen, deduktiven Klassifikationssystems in CPP mit somatischer Beteiligung („specific disease-associated pelvic pain“) sowie CPP ohne eine erklärende somatische Beteiligung („chronic pelvic pain syndrome, CPPS“). Die Letztere ist analog der NIH-Klassifikation IIIB zu verstehen.

Es ist bekannt, dass etwa zwei Millionen Konsultationen bei Urologen in den USA aufgrund dieser Beschwerden geschehen, jedoch nur bei 5-10% der Betroffenen auch eine somatische Verursachung entdeckt werden kann.[8] Diese Daten legen nahe, dass ein Großteil der Patienten und Patientinnen mit unerklärten somatischen Beschwerden vorstellig werden, die als CPPS verstanden werden können. Diese Patientengruppe verursacht hohe Kosten im Gesundheitssystem.[9]
Über die Prävalenzzahlen gibt es sehr heterogene Erkenntnisse. Studienergebnisse über CPPS beim Mann reichen von 2% in Australien[10] bis zu 12% in Nigeria.[11]

Bei Frauen äußert sich das chronische Unterbauchschmerzsyndrom mit ähnlichen Beschwerden und weist z.B. Überlappungen mit dem Krankheitsbild der Interstitiellen Zystitis auf.[12] Auch hier ist das Fehlen einer erklärenden somatischen Beteiligung charakteristisch. Die Prävalenzangaben schwanken ebenfalls beachtlich. Eine Studie in Großbritannien berichtet eine 3-Monats-Prävelenz von 24%, unabhängig von Menstruation, Geschlechtsverkehr oder Schwangerschaft. Etwa 8% der Frauen litten mehr als fünf Jahre unter den Beschwerden.[13] Die Pravalenzraten für Brasilien sind mit 11,5% leicht erhöht.[14] Eine Untersuchung im deutschsprachigen Raum zeigte eine Prävalenzrate bei Frauen von 5,7%, die jedoch im Vergleich zu den männlichen Teilnehmern dieser Studie (2,7%) deutlich höher ist.[15]

Im Gegensatz zu CPPS bei Männern existieren bei Frauen mehr Annahmen über die Verursachung der Beschwerden. Es zeigte sich, dass jeweils mehr als ein Drittel der betroffenen Frauen unter Endometriose[16] oder einem Reizdarmsyndrom[17] leiden. In einer kanadischen Untersuchung konnte die Blase als dominierende Quelle der Schmerzen identifiziert werden.[18] Neuere Ergebnisse deuten auf eine Prävalenzrate bei Frauen mit CPPS von 32% für Interstitielle Zystitis hin.[19] Es konnte nachgewiesen werden, dass ein Großteil der Patientinnen Überlappungen zwischen Beschwerden im Urogenitaltrakt und CPPS aufweisen.[20] Zudem wird CPPS als somatoforme Erkrankung diskutiert. In einer deutschen Studie erfüllten 73,3% der Patientinnen die diagnostischen Kriterien für eine somatoforme Störung.[21] Verschiedene Arbeitsgruppen konnten zeigen, dass der Leidensdruck bei den Betroffenen hoch und die Lebensqualität verringert ist.[22–25]

Klinisches Erscheinungsbild

Die am häufigsten auftretende Form der Chronischen Prostatitis bei Männern ist die Kategorie III der NIH-Klassifikation[26] bzw. das CPPS gemäß der Definition der EAU.[6] Es liegen bisher keine hinreichenden Kenntnisse über die Ätiologie der Erkrankung vor, die dann als Chronic Pelvic Pain Syndrome (CPPS) bezeichnet wird.

Für eine differenzierte Betrachtung einzelner Patienten und Patientinnen sowie zur Einleitung gezielter Therapien wurde die UPOINT-Klassifizierung[27,28] entwickelt. Damit wird der komplexen Symptomdarbietung der Patienten und Patientinnen Rechnung getragen. UPOINT ist das Akronym verschiedener Dimensionen:

- Urinary – Dringlichkeit und Frequenz des Harnlassens sind erhöht. Es erfolgt keine komplette Entleerung der Blase
- Psychosocial – Eine klinisch relevante Depression und katastrophisierende Gedanken sind erkennbar
- Organ specific – Die Prostata / Blase ist druckempfindlich, Leukozyten sind in der Prostataflüssigkeit nachweisbar. Zudem Hämatospermie oder Kalkeinlagerungen in der Prostata. Schmerzen bei Blasenentleerung.
- Infection - Gram-negative bacilli, Enterococcus
- Neurologic/Systemic – Es bestehen weitere Erkrankungen, die eine Erklärung für die CPPS-Symptomatik liefern können (Schmerzen oberhalb von Abdomen und Becken, Reizdarmsyndrom, Fibromyalgie, Chronisches Fatigue Syndrom)
- Tenderness – Fühlbare Verspannungen oder Triggerpunkte im Abdomen und Beckenboden

Bedeutung der Studie vor dem Hintergrund der vorhandenen Studien

CPPS ist ein weit verbreitetes Syndrom, für das es somatischerseits keine hinreichenden ätiologischen Annahmen gibt.[29,30] Gleichzeitig gibt es Hinweise auf ein Zusammenspiel mit psychischen Faktoren[31–33], das sich auch in der Einführung der UPOINT-Klassifizierung widerspiegelt. Die Annahme einer multifaktoriellen Verursachung legt jedoch auch eine multimodale, interdisziplinäre Behandlung nahe, ohne dass bisher effektive Behandlungsansätze identifiziert werden konnten.[34]

Bisherige interdisziplinäre Interventionen basierten bspw. auf der Diagnostik nach dem UPOINT-System.[35] Dabei zeigte sich, dass nur ein Drittel der Patienten mit einer psychosozialen Beeinträchtigung der Empfehlung einer psychotherapeutischen Behandlung im Rahmen der Regelversorgung gefolgt sind.

Ein weiterer Ansatz in den USA bestand in der Kombination von Entspannungsverfahren und Physiotherapie.[36,37] Dieses Vorgehen befindet sich derzeit im Stadium der Pilotstudien und konnte erste Erfolge im Hinblick auf die Schmerzintensität und die Lebensqualität nachweisen, wird jedoch ausschließlich für Männer und ohne Beachtung einer infektiösen Verursachung angewendet. Ebenfalls auf die Behandlung von Männern beschränkt ist das kanadische kognitiv-verhaltenstherapeutische Therapiemodell, welches den Fokus auf die Umstrukturierung katastrophisierender Kognitionen legt.[38] In der Einzelbehandlung zeigte auch hier eine Pilotstudie erste Erfolge durch die Umstrukturierung der dysfunktionalen katastrophisierenden Kognitionen und deren Zusammenhang mit Schmerzintensität und Lebensqualität.[39]

Somit bestehen nur wenige Erkenntnisse über die Effektivität psychotherapeutischer Behandlungen, besonders in Kombination mit anderen Fachdisziplinen. In der im Folgenden beschrieben Behandlung sollen nun beide Geschlechter sowohl psychotherapeutisch als auch physiotherapeutisch behandelt werden. Dabei erlaubt das sequentielle Studiendesign sowohl die Evaluation der einzelnen Komponenten als auch die Evaluation der Kombinationsbehandlung. Die Studie ist damit der erste Ansatz, bei dem Psychotherapie und Physiotherapie kombiniert für Betroffene beiden Geschlechts wissenschaftlich untersucht wird. Die geplante Behandlung in Gruppen stellt darüber hinaus einen ökonomisch sinnvollen Ansatz dar.

Die Zielstellungen der Studie sind:

1) Untersuchung der Machbarkeit einer Kombinationsbehandlung
2) Erfassung der Patientenzufriedenheit
3) Beschreibung der Änderungen hinsichtlich Lebensqualität und Symptomstärke im Verlauf der Studie.
4) Spezifische Wirksamkeit hinsichtlich katastrophisierender Kognitionen und schmerzauslösender Triggerpunkte.

Eigene Vorarbeiten

Die Kooperation der verschiedenen Abteilungen im Universitätsklinikum Hamburg-Eppendorf ermöglicht es, die strukturellen Gegebenheiten optimal zu nutzen und einzubeziehen. So wurde die „Interdisziplinären Forschungsplattform Chronic Pelvic Pain Syndrome (CPPS)“ mit der „Interdisziplinären Spezialsprechstunde CPPS“ im erfolgreich implementiert (vgl. Ethikvotum Berab.Nr. PV4220). Die Patientinnen und Patienten durchlaufen einen diagnostischen Algorithmus (Urologie, Gynäkologie, Psychosomatik sowie im Einzelfall weitere medizinische Disziplinen), der sich bewährt hat. Dabei werden eine Charakterisierung der Patienten nach dem oben geschilderten UPOINT-System und die Diagnostik entsprechend der internationalen Leitlinien durchgeführt. Die interdisziplinäre Zusammenarbeit ist in diesem Zeitraum gewachsen und bildet die Grundlage für die nun geplante Behandlungsstudie. Im Januar 2014 wurde die Pilotphase mit 50 eingeschlossenen Patientinnen und Patienten beendet.

Eine Charakterisierung der Schmerzsymptomatik sowie der psychosomatischen Belastung wurde bereits publiziert.[40] Eine zweite Publikation der Arbeitsgruppe beschäftigt sich mit der theoretischen Herleitung der Kombinationsbehandlung aus Psychotherapie und Physiotherapie anhand der in der Sprechstunde gewonnenen Daten.[41]

3. Ziele und Arbeitsprogramm

3.1 Ziele

Der chronische Beckenbodenschmerz (Chronic Pelvic Pain Syndrome, CPPS) ist eine Erkrankung, die sowohl Männer als auch Frauen betrifft und in ihrer Ätiologie derzeit noch weitgehend unverstanden ist[42–44]. Sowohl die Beschwerden als auch die vermuteten pathogenetischen Mechanismen umfassen verschiedene Organsysteme und sind in ihrem klinischen Bild vielfältig[26,45]. Daraus ergibt sich die Notwendigkeit, auch die Behandlung an diesen verschiedenen Einflussfaktoren zu orientieren.

Es ist das Ziel der 2012 initiierten „Interdisziplinären Forschungsplattform Chronic Pelvic Pain Syndrome (CPPS)“, mehr Aufschluss über die beteiligten somatischen und psychosomatischen Prozesse bei CPPS zu erhalten (vgl. Ethikvotum mit der Bearbeitungsnummer PV4220). Ein weiteres Anliegen der Forschungsplattform ist neben dieser Charakterisierung der Patientenklientel die Entwicklung und Überprüfung geeigneter Behandlungsmethoden.

In der Vergangenheit gab es verschiedene medikamentöse, aber auch nicht-medikamentöse Behandlungsansätze, ohne dass sich eine dieser Behandlungsstrategien bisher als hinreichend hilfreich erwiesen hat.[34,46] Der bisherige Kenntnisstand legt eine interdisziplinäre Behandlungskonzeption nahe.[47]

Es wird daher eine Pilotstudie mit einer kombinierten kognitiv-verhaltenstherapeutischen und physiotherapeutischen Behandlung geplant, um die Machbarkeit dieses Vorgehens zu untersuchen und um erste Anhaltspunkte für eine potentielle Wirksamkeit der Intervention sowie die Planung einer späteren definitiven Therapiestudie zu bekommen.

Aufgrund des explorativen Charakters dieser Pilotstudie und des Fehlens von empirischen Anhaltspunkten zur Durchführung einer Poweranalyse wird für diese Pilotstudie keine Poweranalyse durchgeführt. Die Ergebnisse der Pilotstudie werden für die Planung einer späteren randomisierten, kontrollierten Studie genutzt. Die Ergebnisse der Pilotstudie dienen dann als Basis für die Poweranalyse der späteren definitiven Therapiestudie.

Im Folgenden werden die Forschungsfragen der Therapiepilotstudie definiert.

3.1.1 Gesundheitsbezogene Lebensqualität

Verschiedene Studien zeigen eine deutliche Verringerung der gesundheitsbezogenen Lebensqualität infolge der chronischen Schmerzerkrankung.[22,25,48] Es ist daher im Sinne der Patientinnen und Patienten, eine Verbesserung der Lebensqualität durch die Behandlung zu erreichen.

Hypothese 1: Als primärer Endpunkt wird die Verbesserung der gesundheitsbezogenen Lebensqualität (SF-12)[49] definiert. Zur Katamnese 12 Wochen nach dem Ende der kombinierten Behandlung wird eine Verbesserung der gesundheitsbezogene Lebensqualität in der physischen oder mentalen Skala erwartet.

Begründung: Die einzige bisher vorliegende Untersuchung zur Wirksamkeit der kognitiv-verhaltenstherapeutischen Behandlung berichtete eine Verbesserung der Lebensqualität um 37%.[39] Die Kombination aus Physiotherapie und Entspannungsverfahren zeigte eine Verbesserung der Lebensqualität um 30%.[36] Wir gehen davon aus, dass unsere Kombinationsbehandlung einen ähnlichen positiven Effekt auf die gesundheitsbezogene Lebensqualität bewirkt.

3.1.2 Symptomschwere

Der Chronic Prostatitis Symptom Index des National Institute of Health (NIH-CPSI)[3] gilt international als Maß der Symptomschwere. Es wird angenommen, dass sich die Beschwerden indirekt durch die psychotherapeutischen und direkt durch die physiotherapeutischen Interventionen verringern.

Hypothese 2: Als sekundärer Endpunkt wird die Symptomsschwere (NIH-CPSI)[3] definiert. Zur Katamnese 12 Wochen nach dem Ende der kombinierten Behandlung wird eine Verringerung der Symptomschwere angenommen.

Begründung: Die einzige bisher vorliegende Untersuchung zur Wirksamkeit der kognitiv-verhaltenstherapeutischen Behandlung berichtete eine Reduktion der Symptomschwere um 30%.[39] Die Kombination aus Physiotherapie und Entspannungsverfahren zeigte bei 59% der Teilnehmer eine

Verbesserung der Schmerzsymptomatik um mindestens 25% auf einer visuellen Analogskala und eine Verbesserung der Symptomschwere um 27%.[37] Wir gehen davon aus, dass unsere Kombinationsbehandlung ähnliche Effekte hinsichtlich der Symptomschwere bewirkt.

3.1.3 Weitere psychosoziale und gesundheitsökonomische Parameter

In einer eigenen Untersuchung fanden wir deutlich erhöhte Werte hinsichtlich der psychosozialen Belastung sowie der Inanspruchnahme des Gesundheitssystems.[40] Wir gehen davon aus, dass sich infolge der Therapie Verbesserungen in diesen Variablen ergeben.

Hypothese 3: Als weitere sekundäre Endpunkte wurden kognitive, psychosoziale und ökonomische Parameter gewählt. Das Ausmaß der katastrophisierenden Kognitionen (Pain Catastrophizing Scale)[50] verringert sich um 50%. Depressivität (PHQ-9)[51], Ängstlichkeit (GAD-7)[52], allgemeine somatische Belastung (PHQ-15)[53] und Stresserleben (PSQ)[54] verringern sich. Die Inanspruchnahme des Gesundheitssystems verringert sich hinsichtlich der konsultierten Fachärzte sowie der Fehlzeiten am Arbeitsplatz. Darüber hinaus wird die subjektive Einschätzung der Wirksamkeit der vermittelten Entspannungsmethode (progressive Relaxation) mit einer Visuellen Analogskala (VAS) erhoben.

Begründung: Die einzige bisher vorliegende Untersuchung zur Wirksamkeit der kognitiv-verhaltenstherapeutischen Behandlung berichtete eine Reduktion der schmerzbezogenen katastrophisierenden Kognitionen um 58%.[39] Daten zur Verbesserung depressiver Symptome, von Ängstlichkeit, allgemeiner somatischer Belastung oder vom Stresserleben mittels psychotherapeutischer oder physiotherapeutischer Interventionen liegen für CPPS nicht vor. Gleiches gilt für die gesundheitsökonomische Fragestellung. Allerdings weisen die Patientinnen und Patienten in der Pilotphase der Spezialsprechstunde CPPS im Rahmen der „Interdisziplinären Forschungsplattform Chronic Pelvic Pain Syndrome (CPPS)“ im Vergleich zur Allgemeinbevölkerung in den genannten Variablen deutlich erhöhte Werte auf. Die Wirksamkeit von Entspannungsverfahren bei Schmerzerkrankungen wurde in der Vergangenheit häufig indirekt mittels Symptommaßen erhoben.[55,56] Darüber hinaus zielt der Einsatz der VAS auf eine direkte Messung des vom Patienten wahrgenommenen Effekts ab.

3.1.4 Aufmerksamkeitsfokussierung

Es ist bspw. für Rückenschmerzerkrankungen bekannt, dass die Aufmerksamkeit dieser Patientinnen und Patienten von schmerzrelevanten Reizen gebunden wird.[57] Die verwendete psychotherapeutische Intervention hat einen Fokus auf die Modifikation der schmerzrelevanten Kognitionen. Daher wird eine parallele Reduktion der schmerzbezogenen Aufmerksamkeitsverzerrung infolge der Therapie vermutet.

Hypothese 4: Die kognitive Verarbeitung schmerzbezogener Themen (dargeboten durch Worte) im Sinne einer erhöhten kognitiven thematischen Haftung (bzw. Aufmerksamkeitsfixierung) verringert sich im Prä-Post-Vergleich signifikant. Die erhöhte Aufmerksamkeitsfixierung auf schmerzbezogene Themen wird mit einem computergestützten Experiment („dot-probe-task“) gemessen, das die Reaktionszeit der Patientinnen und Patienten mit einer Serie von neutralen und schmerzbezogenen visuelle dargebotehen Begriffen erfasst. Die Darbietung und Messung erfolgt mit der Software Inquisit™ der Firma Millisecond Software™

Begründung: Das angewendete experimentelle Paradigma der sogenannten „dot-probe-task“[58] hat sich bei chronischen Schmerzerkrankungen bereits bewährt[57,59] und es liegen bspw. Vergleichsdaten für gesunde Probanden und Patienten mit chronischen Rückenschmerzen vor[60]. Es ist daher von einer Aufmerksamkeitshaftung bei CPPS-Patientinnen und Patienten auf schmerzbezogene Themen auszugehen, die durch die kognitiv-verhaltenstherapeutische Intervention reduziert wird.

3.1.5 Veränderungsmessung infolge der Physiotherapie

Die physiotherapeutische Behandlung basiert u.a. auf der gemeinsamen Vereinbarung von Zielen. Es ist daher anzunehmen, dass ein Zusammenhang zwischen dem wahrgenommenen Erfolg der Therapie und dem Erreichen der Ziele besteht. Da es bislang noch keine spezifischen Endpunkte für die physiotherapeutische Intervention gibt, sollen weitere Parameter (v.a. Anzahl der Triggerpunkte) auf ihren Nutzen zur Erfassung von Veränderungen hin untersucht werden.

Hypothese 5: Ergänzend zu den genannten Zielparametern wird die Wirksamkeit der Physiotherapie mit der Goal Attainment Scale (GAS)[61] gemessen. Als weiteres Beschwerdemaß werden die Anzahl und das Ausmaß des Schmerzes relevanter myofaszialer Triggerpunkte erhoben. Da keine Referenzdaten für die

physiotherapeutische Behandlung des CPPS vorliegen, werden a-priori keine Angaben zu erwarteten Veränderungen postuliert.

Begründung: Das Vorgehen der physiotherapeutischen Behandlung sowie erste Ergebnisse zur Wirksamkeit sind durch das „Stanford-Protokoll“ beschrieben.[37] In dieser Studie zeigte sich, dass 68 der befragten 92 Patienten (von ursprünglich n = 138) ihren Zustand nach der Behandlung als stark bis mäßig verbessert einschätzten. Daher erscheint uns ein Wert von 50% Zielerreichung als realistische und erstrebenswerte Größe.
Die relevanten Triggerpunkte wurden in der Untersuchung ebenfalls identifiziert[62], jedoch liegen noch keine empirische Daten über deren Veränderung infolge einer Therapie vor.

3.1.6 Annahme der Intervention

Die eingesetzten Behandlungsansätze sind in der Vergangenheit im deutschsprachigen Gebiet noch nicht genutzt worden. Für die weitere Untersuchung im Rahmen einer definitiven randomisiert-kontrollierten Therapiestudie sowie für eine zukünftige Implementierung in die Versorgungslandschaft ist die Erhebung der Patientenzufriedenheit bedeutsam. Außerdem soll die Sichtweise der Patientinnen und Patienten genutzt werden, um Veränderungen an einzelnen Bausteinen der Intervention vorzunehmen.

Hypothese 6: Die Zufriedenheit sowie die Bereitschaft zur Weiterempfehlung an andere Betroffene werden mittels einer zehnstufigen Visuellen Analog-Skala erhoben.

Begründung: Die Daten der Pilotphase der Spezialsprechstunde CPPS im Rahmen der „Interdisziplinären Forschungsplattform Chronic Pelvic Pain Syndrome (CPPS)“ haben bereits gezeigt, dass Patientinnen und Patienten einen hohen Leidensdruck haben und zumeist langjährige auf der Suche nach einer adäquaten Behandlung sind.[63] Die Akzeptanz der zu untersuchenden Behandlung ist daher im Sinne einer Machbarkeitsstudie ein wichtiger Outcome-Parameter.

3.2 Arbeitsprogramm

3.2.1 Studiendesign

Bei der geplanten Untersuchung handelt es sich um eine Pilotstudie, die an das Design eines „Cohort Multiple randomised controlled trials“[64] angelehnt ist (vgl. Abb. 1). Dieses Studiendesign wurde speziell für Behandlungsstudien konzipiert, deren Teilnehmer sich aus Kohortenuntersuchungen rekrutieren. Für unsere Pilotstudie werden somit die Patienten / -innen aus der Stichprobe der Patienten/ -innen der Beobachtungsstudie zur „Interdisziplinären Spezialsprechstunde CPPS“ (PV4220) gewonnen. Die Zuteilung auf Behandlungs- und Kontrollgruppe wird nicht randomisiert vorgenommen, sondern wird durch die Möglichkeit zur regelmäßigen Präsenz am Behandlungsort (Universitätsklinikum Hamburg Eppendorf) definiert.

Durch diese Gruppenzuteilung ist eine Auswertung sowohl in einem Within- als auch in einem Between-Subject-Design möglich. Alle Patienten/ -innen der Beobachtungsstudie zur „Interdisziplinären Spezialsprechstunde CPPS“ haben bereits bei ihrer Vorstellung in der Sprechstunde zu einer einjährigen Katamnese eingewilligt (siehe Antrag zum Ethikvotum PV3842), so dass die Nachbefragung bereits im Rahmen der Beobachtungsstudie realisierbar ist.

Die eingeschlossenen Patienten/-innen erhalten im ersten Behandlungsschritt nach einer Auftaktsitzung eine kognitiv-verhaltenstherapeutisch orientierte Gruppentherapie (durchschnittlich 6 Teilnehmer, geschlechtshomogene Gruppenzusammensetzung) mit einer 90-minütigen wöchentlichen Sitzung über 9 Wochen. Die Behandlung wird von einem geschulten Therapeuten sowie einem Ko-Therapeuten (Diplom-Psychologe oder Arzt) durchgeführt und liegt manualisiert vor. Das Manual wurde von unserer Arbeitsgruppe erstellt und basiert auf den Vorarbeiten einer kanadischen Arbeitsgruppe.[38] Die einzelnen Elemente der kognitiv-verhaltenstherapeutischen Behandlung sind in Tabelle 1 dargestellt.

Neben dem Fokus auf die Umstrukturierung der katastophisierenden Kognitionen ist auch eine Vermittlung von Progressiver Relaxation vorgesehen. In jeder Sitzung ist eine Therapieeinheit zur Anwendung dieser Entspannungstechnik vorgesehen. Aktuelle Studien belegen die Wirksamkeit der Progressiven Relaxation bei Schmerzerkrankungen. [55,56]

An den 12-wöchigen Katamnesezeitraum der psychotherapeutischen Behandlungsphase schließt die physiotherapeutische Behandlung als zweite Stufe des Therapieplans an. Es handelt sich um eine adaptierte Behandlung des bisher für CPPS am besten evaluierten Ansatzes einer kombinierten Behandlung aus Physiotherapie und Entspannungsverfahren.[37,65] Drei Sitzungen finden in der Gruppenzusammensetzung der ersten Behandlungsstufe statt (90 min), während die restlichen 5 Termine im Rahmen einer 60minütigen Einzelbehandlung durchgeführt werden. Die einzelnen Elemente der phyiotherapeutischen Behandlung sind in Tabelle 2 dargestellt.

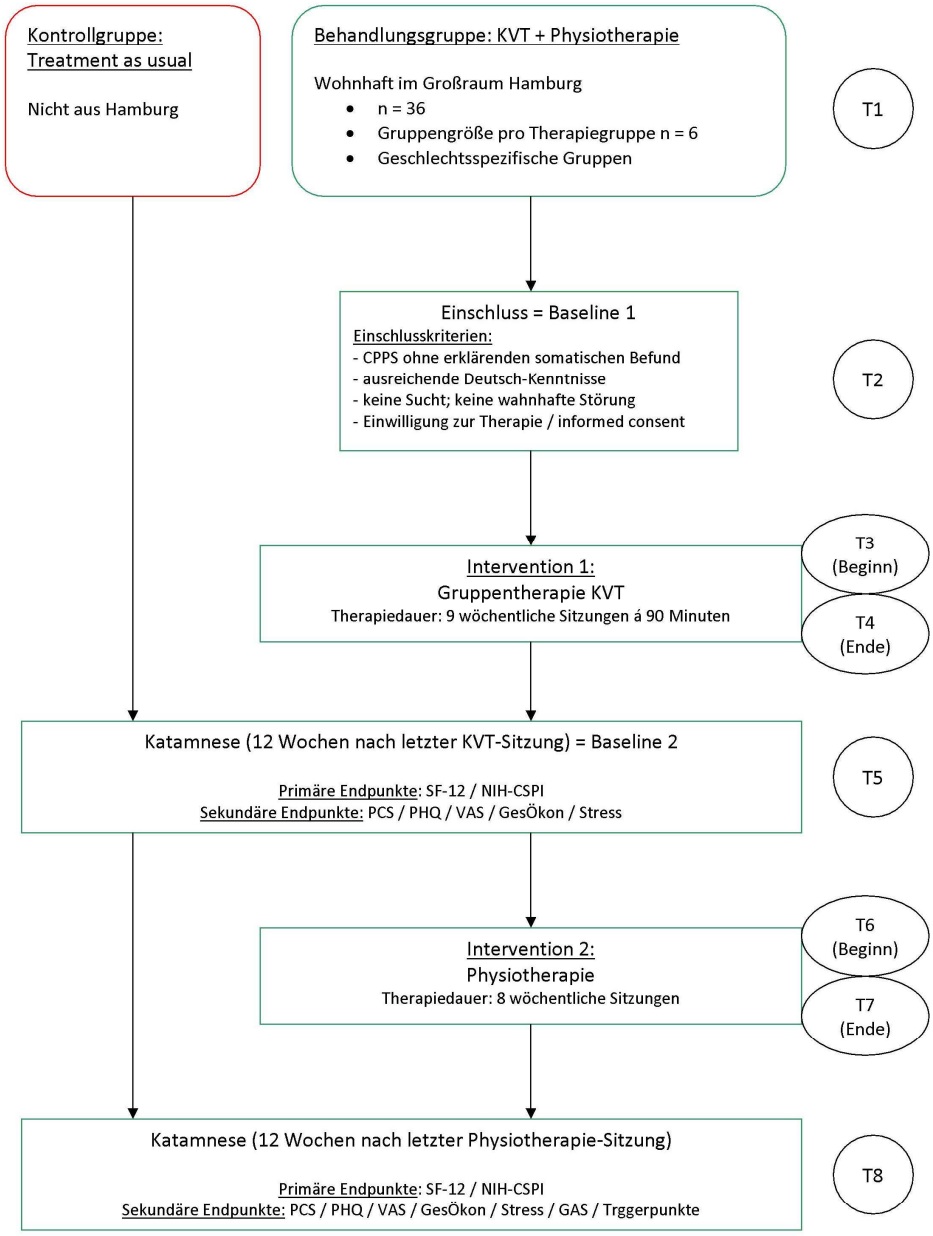

Abbildung 1: Flow-Chart zum Ablauf der Pilotstudie

Tabelle 1: Ablauf und Inhalt der psychotherapeutischen Behandlung

Therapie-Einheit	Behandlungs-art	Inhalt
1	Gruppe	• Einführung zu Inhalten des Programms: Schmerz, Beeinträchtigung, Bewältigung, Stimmung, Unterstützung • Verhaltensanalysen; Rolle des Patienten innerhalb des Programms: „Experte seiner Erkrankung“ der aktiv mitarbeiten muss; Hausaufgaben als zentraler Bestandteil; • Einführung in Progressive Relaxation (PR)
2	Gruppe	• Gruppendiskussion • Ausführliche Übung der PR • Verhaltensanalyse
3	Gruppe	• Gruppendiskussion • Ausführliche Übung der PR • Einführung „Katastrophisierende Gedanken“ • Verhaltensanalysen in Kleingruppen erarbeiten
4	Gruppe	• Gruppendiskussion • Verkürzte Übung der PR • Negative Selbstbotschaften in Kleingruppen erarbeiten • Verhaltensanalysen in Großgruppe vertiefen
5	Gruppe	• Gruppendiskussion • Verkürzte Übung der PR • Theorie: Einfluss sozialer Beziehungen • „Ich-Botschaften“ modifizieren • Verhaltensanalysen in Kleingruppen mit Fokus auf soziale Interaktion
6	Gruppe	• Gruppendiskussion • Verkürzte Übung der PR • Vertiefung: Einfluss sozialer Beziehungen / Suche nach Unterstützern • „Zuhörerfertigkeiten“ thematisieren • Verhaltensanalysen
7	Gruppe	• Gruppendiskussion • Verkürzte Übung der PR • Theorie: Copingstrategien • Positive Selbstbotschaften als Copingstrategie entwickeln • Verhaltensanalysen
8	Gruppe	• Gruppendiskussion • Verkürzte Übung der PR • Vertiefung: Copingstrategien • Balance „Aktivität / Inaktivität“ verbessern / Erkennen von Vermeidungsverhalten / Stimulieren körperlicher Aktivität • Verhaltensanalysen
9	Gruppe	• Gruppendiskussion • Verkürzte Übung der PR • Bewertung der eigenen Veränderungen im Verlauf des Behandlungsprogramms • Wiederholung der Inhalte • Abschied

Tabelle 2: Ablauf und Inhalt der physiotherapeutischen Behandlung

Therapie-Einheit	Behandlungs-art	Inhalt
1.Einheit (90 Min.)	Gruppe	• *Informationsvermittlung:* Zusammenhang zwischen Muskelspannung, Stress und Schmerz • *Selbsterfahrungen:* Wahrnehmung von An- und Entspannung der Beckenbodenmuskulatur • *Anleitung zu Eigenübungen* • *Zielformulierung (GAS)*
2.Einheit (60 Min.)	Einzel	• *Reflektorische Atemtherapie*® • *Eigenübung* entsprechend der Atemreaktion bzw. des Befundes • *Wahrnehmungsschulung* vorher/nachher
3. + 4. Einheit (60 Min.)	Einzel	• Einstieg: Reflexion der bisherigen Erfahrung • *Reflektorische Atemtherapie*® • *Eigenübung* entsprechend der Atemreaktion bzw. des Befundes • *Wahrnehmungsschulung* vorher/nachher
5.Einheit (90 Min.)	Gruppe	• Einstieg: Reflexion der bisherigen Erfahrung in der Gruppe • *Eigenübung* intensivieren • *Angeleitete Übung:* gemeinsame therapeutische Körperstellungen
6.Einheit (60 Min.)	Einzel	• Einstieg: Reflexion der bisherigen Erfahrung • *Reflektorische Atemtherapie*® • *Eigenübung* entsprechend der Atemreaktion bzw. des Befundes • Einführung der *„Arbeit mit dem Schmerz“* • *Wahrnehmungsschulung* vorher/nachher
7.Einheit (I) (60 Min.) + (II) (30 Min)	Einzel	• Einstieg: Reflexion der bisherigen Erfahrung • *Reflektorische Atemtherapie*® • *Eigenübung* entsprechend der Atemreaktion bzw. des Befundes • Weiterführung der *„Arbeit mit dem Schmerz“* • *Wahrnehmungsschulung* vorher/nachher
	Einzel	• *Feedbackgespräch* zur Einzeltherapie • *Ziele überprüfen und einordnen* • *Planen des Eigenmanagements* • Aufgabe zur abschließenden Gruppenstunde: *Reflexion* der bisherigen Zielerreichung
8.Einheit (90 Min.)	Gruppe	• *Reflexion* der bisherigen Zielerreichung in der Gruppe • *Planung* zur Fortführung der Eigenübungen • Gemeinsame therapeutische Körperstellungen • Abschluss

Die Auswertung der Pilotphase unserer Spezialsprechstunde zum Chronischen Unterbauchschmerzsyndrom am Universitätsklinikum Hamburg Eppendorf zeigt, dass die Patientinnen und Patienten von allen erfragten Therapieversuchen in der Vergangenheit am ehesten die Physiotherapie als hilfreich erlebten.[41] Allerdings ist kein Therapieansatz bisher ausreichend evaluiert. Eines der am besten beschriebenen Therapiekonzepte ist das Wise-Anderson-Protokoll.[37] Neben physiotherapeutischen Maßnahmen zur strukturellen Behandlung von myofaszialen Triggerpunkten, nutzen die Autoren eine Atemtechnik, das „Respiratory Sinus Arrhythmia breathing (RSA breathing)“[65] in Kombination mit einem Entspannungsverfahren unter gleichzeitiger Anleitung der Patienten zur Eigenbehandlung und

Eigenübung. Bisher wurde dieses Verfahren jedoch nur bei Männern angewendet. Die Übertragung der Methodik auf Frauen mit CPPS ist dagegen ein neuer Aspekt. Damit zielt unsere Studie auch auf eine Erweiterung der Anwendungsmöglichkeiten ab.
Die physiotherapeutische Intervention dieser Studie setzt sich in Anlehnung an das Wise-Anderson-Protokoll aus folgenden Elementen zusammen:

- Aufklärung der Patienten über
  - die Anatomie,
  - Funktion des Bewegungsapparates/Haltung speziell auch des Beckenbodens und des Zwerchfells,
  - den Einfluss von Stress auf den Muskeltonus und die Steifigkeit von Faszien
  - die Notwendigkeit der Selbstbehandlung und der Durchführung des Eigenübungsprogramms
- Wärmeanwendung
- Manuelle Behandlung der myofaszialen Triggerpunkte
- Beeinflussung der Zwerchfellaktivität
- Instruktion des Patienten in der Eigenbehandlung und Begleitung des Eigenübungsprogramms

Ergänzend zu dem vorgegebenen Protokoll werden Zielvereinbarung mit den Patientinnen und Patienten erarbeitet.[66] Die gemeinsam erarbeiteten Ziele werden mit Hilfe der Goal Attainment Scale (GAS) gemessen (-2 bis +2).[61]

Ein Behandlungskonzept der Physiotherapie, das die meisten der im Anderson Wise Protokoll benannten Aspekte berücksichtigt, ist die Reflektorische Atemtherapie®.[67,68] Dieses Therapiekonzept wirkt durch Einsatz von manuellen Techniken direkt an allen Strukturen des Bewegungsapparates (Muskeln, Sehnen, Gelenke, Periost und Faszien) und reflektorisch auf die Zwerchfellaktivität. Neben den manuellen Techniken nutzt die Reflektorische Atemtherapie® die Wirkung von Wärme in Form von heißen Tüchern, die auf den Körper appliziert werden. Die „therapeutischen Körperstellungen“ – das dritte Element in der Reflektorischen Atemtherapie® - entsprechen dem Eigenübungsprogramm: Die Patienten erhalten je nach individueller Notwendigkeit eine bis drei Eigenübungen. Mit diesen täglich durchzuführenden Übungen wird die Eigenaktivität unterstützt und die in der Einzelbehandlung erreichten Änderungen werden gefestigt. Die im Wise-Anderson-Protokoll beschriebene paradoxe Muskelrelaxation wird durch die Erfahrung und Wahrnehmungsschulung ersetzt, die durch den Einsatz der Reflektorischen Atemtherapie® erreicht wird.

An die letzte Sitzung der physiotherapeutischen Behandlung schließt sich ein 12-wöchiger Katamnesezeitraum an.

3.2.2 Erhebungsinstrumente

Die Datenerhebung während des ersten Messzeitpunkts (Sprechstunde) wurde bereits im vorhergehenden Ethikantrag beschrieben.

In Abbildung 2 sind die genutzten Messinstrumente den einzelnen Messzeitpunkten zugeordnet. Im Einzelnen handelt es sich um folgende, psychometrisch hinreichend untersuchte Verfahren:

Ein Teil der Messinstrumente wird bereits im Rahmen der Spezialsprechstunde eingesetzt. Neben der Krankheitsanamnese, den soziodemographischen Daten sowie einem Fragebogen zur Inanspruchnahme des Gesundheitssystems werden die CPPS-relevanten Symptome mit der deutschen Version des National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) erfasst. Es handelt sich um ein international anerkanntes Messinstrument zur Erhebung der Beschwerden bei CPPS[69] und liegt in einer deutschen Übersetzung mit guten psychometrische Kennwerten vor[5]. Der NIH-CPSI umfasst neun Items auf drei Skalen (Schmerz, urologische Symptome, Lebensqualität). Für jede Skala kann ein Summenwert errechnet werden. Der Summenwert der drei Skalen bildet den Gesamtwert.
Das Schmerzerleben wird mit der deutschen Version[70] der Short-Form McGill Pain Questionnaire (SF-MPQ) erhoben[71]. Der Schmerz wird mit 15 Adjektiven beschrieben und in seiner Intensität auf einer vierstufigen Skala eingeschätzt. Die Gesamtskala teilt sich in zwei Subskalen mit 11 Items zur sensorischen Qualität und 4 Items zur affektiven Qualität des Schmerzerlebens auf.

Die Beeinträchtigung im Lebensalltag durch die Schmerzerkrankung wird mit dem Pain Disability Index (PDI)[72] erfasst. Es handelt sich um ein häufig eingesetztes, ökonomisches Instrument mit sieben Items.
Die gesundheitsbezogene Lebensqualität (englisch: Quality of Life (QoL)) wird mit der deutschen Version des gut evaluierten 12-Item Short Form Health Survey (SF-12) gemessen, der mit Hilfe von zwölf Items eine körperliche Summenskala (PCS) und eine psychische Summenskala (MCS) ermittelt.[49]
Der ebenfalls gut evaluierten Patient Health Questionnaire (PHQ-D) wird eingesetzt, um die psychische Belastung zu quantifizieren. Dafür werden folgende drei Module genutzt: Die Subskala PHQ-9 besteht aus neun Items und misst den Schweregrad einer Major Depression.[51] Der PHQ-15 erfasst mit 15 Items den Schweregrad somatischer Symptome.[53] Die Generalized Anxiety Disorder Scale (GAD-7) ist das aus sieben Items bestehende Modul zur Erfassung der generalisierten Angststörung bzw. der Symptomschwere der allgemeinen Ängstlichkeit.[52]
Das Ausmaß der schmerz-katastrophisierenden Gedanken wird mit der Pain Catastrophizing Scale (PCS) erfasst.[50] Der Fragebogen umfasst 13 Items und besitzt eine ausreichende psychometrische Güte.[73] Die erhöhte Aufmerksamkeit für schmerzbezogene Reize wird mit Hilfe des „dot-probe-paradimas“[58] erfasst und mittels der dafür entwickelten Software Inquisit™ der Firma Millisecond Software™ gemessen.
Die Zielerreichung in der Physiotherapie wird mit Hilfe der Goal Attainment Scale (GAS), einem gängigen Verfahren zur Zielmessung, auf einer Skala von -2 bis +2 quantifiziert.[61]

Tabelle 3: Verwendete Messinstrumente zu den einzelnen Messzeitpunkten

Messinstrument	**Sprech-stunde** **t1**	**Ein-schluss** **t2**	**Beginn KVT** **t3**	**Ende KVT** **t4**	**Follow-up KVT** **t5**	**Beginn Physio** **t6**	**Ende Physio** **t7**	**Follow-up Physio** **t8**
Soziodemographische Angaben, Anamnese	X							
Inanspruchnahme des Gesundheitssystems	X	X		X	X		X	X
Urologische Symptomatik ***(NIH-CPSI)***	X	X	X	X	X	X	X	X
Schmerzwahrnehmung ***(SF-MPQ)***	X	X	X	X	X	X	X	X
Einschränkungen durch Schmerz ***(PDI)***		X	X	X	X	X	X	X
Gesundheitsbezogene Lebensqualität ***(SF-12)***	X	X	X	X	X	X	X	X
Psychische Belastung ***(PHQ-9, PHQ-15, GAD7)***	X	X	X	X	X	X	X	X
Katastrophisierende Kognitionen ***(PCS)***	X	X	X	X	X	X	X	X
Stresserleben ***(PSQ)***	X	X	X	X	X	X	X	X
Behandlungszufriedenheit					X			X
Interview: Psychische Störungen ***(SKID-I)***	X							
Erhöhte Aufmerksamkeit für schmerzbezogene Reize ***(dot-probe-task)***			X	X	X			
Zielerreichung Physiotherapie ***(GAS)***							X	X

3.2.3 Untersuchungsablauf

Die Studie wird am Universitätsklinikum Hamburg-Eppendorf durchgeführt. Sowohl die Koordination der Sprechstunde als auch die Koordination der beiden Therapiemodule obliegen dem Institut und der Poliklinik für psychosomatische Medizin und Psychotherapie unter Leitung von Prof. Dr. Bernd Löwe. Die oben geschilderte Pilotstudie versteht sich dabei als Projekt welches eine konsequente Weiterentwicklung der Interdisziplinäre Spezialsprechstunde „Chronic Pelvic Pain Syndrome (CPPS)“ darstellt.

Die Patientinnen und Patienten der Therapiestudie werden im Rahmen der Spezialsprechstunde „Chronic Pelvic Pain Syndrome (CPPS)“ rekrutiert. Als Einschlusskriterien werden ein Mindestalter von 18 Jahren sowie die Diagnose eines CPPS gemäß den Forschungskriterien für Männer[29] bzw. den Kriterien für die Diagnose eines CPPS für Frauen[30] definiert:

Diagnose CPPS bei Männern:

- Schmerzen im Urogenitaltrakt
- Beschwerden bestehen seit mehr als sechs Monaten
- Zusatzsymptomatik: Blasenentleerungsstörung, sexuelle Dysfunktion, Reizdarmsyndrom
- Fehlender Nachweis einer bakteriellen Verursachung

Diagnose CPPS bei Frauen:

- Schmerzen im Urogenitaltrakt
- Beschwerden bestehen seit mehr als sechs Monaten
- Zusatzsymptomatik: gynäkologische oder sexuelle Dysfunktion, Dysfunktion im Darm
- Fehlender Nachweis einer bakteriellen Verursachung

Darüber hinaus wird eine Minderung der gesundheitsbezogenen Lebensqualität (SF-12) entweder hinsichtlich des physischen (PCS) oder des mentalen (MCS) Summenscores um eine Standardabweichung (10 Punkte) als Einschlusskriterium definiert.

Als Ausschlusskriterien wird eine bestehende Substanzabhängigkeit mit der Ausnahme von Tabak und Schmerzmittelabusus festgelegt. Außerdem stellen akute Suizidalität und eine produktive psychotische Symptomatik Ausschlussgründe dar. Des Weiteren müssen die Sprachkenntnisse für das Verständnis des Informed Consent ausreichen.

Methodik der Erhebungen: Es werden ausschließlich Patienten und Patientinnen in die Therapiestudie eingeschlossen, die im Rahmen des Erstgesprächs eine schriftliche Einwilligungserklärung nach erfolgter Aufklärung abgegeben haben.

Die Rekrutierung der Probanden erfolgt vorwiegend durch die „Interdisziplinäre Sprechstunden Chronic Pelvic Pain Syndrome (CPPS)“ (PV 4220). Darüber hinaus ist auch eine Rekrutierung von Patienten und Patientinnen über ein Netzwerk kooperierender niedergelassener Fachärzte geplant. Der Einschluss in die Studie bedingt eine vorangegangene ausführliche somatische Untersuchung, um eine somatische Verursachung des Schmerzsyndroms auszuschließen.

Als Ausschlusskriterien für eine Teilnahme an der Therapiestudie wird eine bestehende Substanzabhängigkeit mit der Ausnahme von Tabak und Schmerzmittelabusus definiert. Außerdem stellen akute Suizidalität und eine produktive psychotische Symptomatik Ausschlussgründe dar. Des Weiteren müssen die Sprachkenntnisse für das Verständnis des Informed Consent ausreichen.

3.2.4 Poweranalyse

Aufgrund des explorativen Charakters dieser Pilotstudie und des Fehlens von empirischen Anhaltspunkten zur Durchführung einer Poweranalyse wird für diese Pilotstudie keine Poweranalyse durchgeführt. Die Ergebnisse der Pilotstudie werden für die Planung einer späteren randomisierten, kontrollierten Studie genutzt. Die Ergebnisse der Pilotstudie dienen dann als Basis für die Poweranalyse der späteren definitiven Therapiestudie.

3.2.5 Statistische Auswertung

Die erhobenen psychometrischen und symptombezogenen Variablen werden in einem Prä-Post-Vergleich ausgewertet. Darüber hinaus werden mittels regressionsbasierter Methoden Aussagen über förderliche und hinderliche Faktoren für den Therapieerfolg getroffen.

3.2.6 Zeitlicher Ablauf

Die Datenerhebung beginnt unmittelbar nach dem Eingang des Ethikvotums und soll in einem Zeitraum von 18 Monaten abgeschlossen werden.

3.3 Untersuchungen am Menschen oder an vom Menschen entnommenem Material

Die Empfehlungen des Weltärztebundes (revidierte Deklaration von Helsinki 2000) sind bei der Planung dieser Untersuchung beachtet worden. Bei der beantragten Studie handelt es sich um eine prospektive Kohortenstudie und keinen Heilversuch.

Mögliche Risiken und Vorsorgemaßnahmen: Risiken oder Kontraindikationen durch die geplante Untersuchung sind nicht bekannt, da es sich um eine psychologische Studie mit Einsatz von schriftlich oder mündlich abgefragten Fragebogenverfahren sowie standardisierten, strukturierten diagnostischen Interviews handelt. Es liegt eine Expertise hinsichtlich der sicheren Anwendung und Auswertung dieser Verfahren auf Seiten der Projektleiter und –mitarbeiter vor. Alle teilnehmenden Patienten erhalten das Angebot, sich bei Bedarf in den Ambulanzen der teilnehmenden Institute des Universitätsklinikums Hamburg-Eppendorf vorzustellen.

Im Rahmen des Depressionsfragebogens PHQ-9 fragt ein Item nach Todeswünschen bzw. Suizidphantasien der Probanden. Es ist jedoch gut belegt, dass sowohl die Anwendung von psychologischen Fragebögen als auch die Frage nach Suizidalität das tatsächliche Suizidrisko nicht erhöhen, sondern eher vermindern.[74] Es wird nicht in weitergehende medizinische Behandlungsabläufe eingegriffen, so dass keine gesundheitlichen Risiken durch die Untersuchung bestehen. Zur Klärung potentieller Fragen steht den Probanden wochentags zwischen 8:00 Uhr und 16:30 Uhr die Möglichkeit eines Telefonkontaktes mit einem Studienmitarbeiter zur Verfügung. Für alle gesundheitlichen Fragen, die mit einer möglichen Erkrankung verbunden sein könnten, steht den Probanden jederzeit die medizinische Versorgung durch die teilnehmenden Institute am Universitätsklinikum Hamburg-Eppendorf zur Verfügung.

Während der Behandlung kann es zu einer Verstärkung der Schmerzen oder der depressiven Symptomatik bis hin zu suizidalen Verhaltensweisen kommen. In diesem Fall ist ein Gespräch mit dem zuständigen Oberarzt vorgesehen, in dem dann das weitere Vorgehen (Abbruch der Studienbehandlung, Einleitung anderer Behandlungsoptionen) besprochen wird.

Art der Probandenaufklärung und Einholung des Einverständnisses: Entsprechend wissenschaftlichen Konventionen werden die Probanden in schriftlicher Form vollständig über die Untersuchung aufgeklärt und dokumentieren ihre freiwillige Teilnahme (s. Anlage). Wenn sich die Patienten in der Ambulanz des Universitätsklinikums Hamburg-Eppendorf vorstellen, erhalten sie zusätzlich eine mündliche Aufklärung zur Studienteilnahme. Alle Patienten erhalten eine Telefonnummer am Institut des Studienleiters mitgeteilt, unter der sie mit einem wissenschaftlichen Mitarbeiter der Studie verbunden werden können und ihre Fragen beantwortet bekommen (Sekretariat, Tel: 040-7410-59733). Die Teilnahme an der Untersuchung kann jederzeit ohne Angabe von Gründen seitens der Probanden abgebrochen werden und zieht für den Probanden keine negativen Konsequenzen nach sich.

3.4 Tierversuche

entfällt

3.5 Gentechnologische Experimente

entfällt

3.6 Forschungen, die unter das Übereinkommen über die biologische Vielfalt (Convention on Biological Diversity - CBD) fallen

Entfällt

3.7 Umgang mit den im Projekt erzielten Forschungsdaten

Nach Abschluss der Datenerhebung werden die nicht elektronisch erfassten Daten in eine Datenbank eingegeben und mit den elektronisch erfassten Daten anhand einer Studiennummer zusammengeführt. Die Datenbank wird keine persönlich identifizierbaren Informationen enthalten. Nach Abschluss der Eingabe der Rohdaten wird die Datenbank auf CDs gebrannt werden und gemeinsam mit den übrigen pseudonymisierten Papierdokumenten für mindestens 5 Jahre nach Studienabschluss an einem gesicherten Ort in der Studienzentrale aufbewahrt. Die Fragebögen werden ohne persönlich identifizierbare Informationen in einem verschlossenen Schrank im Institut und der Poliklinik für Psychosomatische Medizin und Psychotherapie (UKE) aufbewahrt. Der „Datenschlüssel“, welcher die Zuordnung von Probanden zu den pseudonymisierten Daten ermöglicht, wird davon getrennt in einem ebenfalls verschlossen Schrank im Institut und der Poliklinik für Psychosomatische Medizin und Psychotherapie (UKE) verwahrt. Alle erhobenen Daten werden getrennt vom „Datenschlüssel“ aufbewahrt. Die Daten können kooperierenden Wissenschaftlern für spezifische Fragestellungen auf Anfrage in pseudonymisierter zur Verfügung gestellt werden.
Die Ergebnisse dieses Projektes werden anderen Wissenschaftlern durch Publikationen frühzeitig zur Verfügung gestellt. Es wird eine interdisziplinäre Zusammenführung der wissenschaftlichen Erkenntnisse mit den übrigen beteiligten Einrichtungen angestrebt.

4. Unterschrift der ärztlichen Studienleitung

Hamburg, 10. Juli 2014

5. Verzeichnis der Anlagen

- Literaturverzeichnis
- Patienteninformation
- Einverständniserklärung
- Patientenfragebogen:

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CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility trial in the title	1
	1b	Summary of pilot trial design, methods, results, and conclusions	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for pilot trial	5-6
	2b	Specific objectives or research questions for pilot trial	5-6
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	6-7
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	7-8
	4b	Settings and locations where the data were collected	6-7
	4c	How participants were identified and consented	7-8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8-9
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	9-10
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	N/A
Sample size	7a	Rationale for numbers in the pilot trial	N/A
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	N/A
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	N/A
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	N/A
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to	N/A

		interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	Figure 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	12
	14b	Why the pilot trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	Figure 1
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	12-14 Tables 2-4
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	15-19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	16-17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	15-17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	18-19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	7
Protocol	24	Where the pilot trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	20
	26	Ethical approval or approval by research review committee, confirmed with reference number	7

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Trials

STUDY PROTOCOL

Open Access

Combined Cognitive-Behavioural and Physiotherapeutic Therapy for Patients with Chronic Pelvic Pain Syndrome (COMBI-CPPS): study protocol for a controlled feasibility trial

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Abstract

Background: Chronic pelvic pain syndrome (CPPS) is a pain condition perceived in the pelvic area for at least 6 months. While evidence of the aetiology and maintenance of CPPS is still unclear and therapy options are rare, there is preliminary evidence for the efficacy of cognitive behavioural therapy and physiotherapy. However, an integrated treatment has not yet been studied. The primary aim of this study is therefore to test the feasibility of combined psychotherapy and physiotherapy for female and male patients with CPPS. The secondary aim is to explore changes in patient-relevant and economic outcomes compared to a control group.

Methods: A feasibility study with a crossover design based on the principles of a 'cohort multiple randomized controlled trial' will be conducted to test a combined therapy for patients with CPPS. The study will consist of two consecutive treatment modules (cognitive behavioural group psychotherapy and physiotherapy as individual and group sessions), which will be applied in varying order. The modules will consist of nine weekly sessions with a 4-week break between the modules. The control group will undergo treatment as usual. Study subjects will be recruited from the interdisciplinary outpatient clinic for CPPS at the University Medical Center Hamburg-Eppendorf. Thirty-six patients will be assigned to the intervention, and 18 patients will be assigned to the control group. The treatment groups will be gender homogeneous. Feasibility as the primary outcome will be analysed in terms of the demand, acceptability, and practicality. Secondary study outcomes will be measured using validated self-rating-scales and physical examinations.

Discussion: To the best of our knowledge, this study is the first to investigate the feasibility of combined psychotherapy and physiotherapy for patients with CPPS. In addition to testing feasibility, the results can be used for the preliminary estimation of therapeutic effects. The results from this study will be used to generate an enhanced therapeutic approach, which might be subject to further testing in a larger study.

(Continued on next page)

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(Continued from previous page)

Trial registration: German Clinical Trials Register, DRKS00009976. Registered on 15 March 2016. ISRCTN, ISRCTN43221600. Registered on 10 May 2016.

Keywords: Chronic pelvic pain syndrome, Chronic pain, Cognitive behavioural therapy, Group psychotherapy, Physical therapy modalities, Feasibility studies

Background

Chronic pelvic pain syndrome (CPPS) can be described as an intermittent or constant pain condition in the pelvic area that has persisted for at least 6 months without an obvious pathology that accounts for the pain [1]. It is associated with physical symptoms suggestive of gastroenterological, urogenital, and/or sexual dysfunction [1–3] as well as with psychopathological symptoms and a reduced health-related quality of life [1, 4–15]. Psychological correlates are also emphasized by clinical phenotyping systems, such as UPOINT [16]. Thirty-four to 37% of the patients with CPPS have positive findings in the UPOINT domain 'psychosocial dysfunction'. Furthermore, 53–64% of the patients have findings in the 'tenderness of muscles' domain [17, 18], suggesting that psychotherapy and physiotherapy might be important in the treatment of patients with CPPS.

CPPS is a common pain condition with international general population prevalence rates ranging between 4 and 25% in women [8, 19–21] and between 2 and 18% in men [22–24].

Although CPPS is common, the aetiology and maintenance of CPPS are still largely unknown [25–29] and the successful management of this pain syndrome remains challenging [30, 31]. Several single-track medical and non-medical treatment strategies have failed to be sufficient [31, 32]. Therefore, a multidisciplinary approach combining medical, psychotherapeutic, and physiotherapeutic treatment strategies is recommended [1, 18, 33]. However, some psychotherapeutic and physiotherapeutic treatment strategies have shown promising effects. Cognitive behavioural therapy (CBT) strategies seem to reduce pain and symptom severity as well as increase the quality of life [34–36]. Myofascial physiotherapy techniques alone or in combination with breathing and relaxation techniques appear to be effective for treating urinary and sexual symptoms, pain, and quality of life [37–41].

Objectives

Regarding the advocacy for multimodal therapy established in the guidelines of the European Association of Urology (EAU) [1], there is an urgent need to examine combined interventions for patients with CPPS. However, due to constraints of resources, not all interventions can be tested for efficacy and effectiveness. In this case, a feasibility study can be used to decide whether a treatment method is worth further investigation and whether changes should be applied to the intervention [42].

Therefore, the primary aim of this study is to explore the feasibility of a combined psychotherapeutic and physiotherapeutic treatment for both female and male patients with CPPS. The results from this study will be used to generate an enhanced therapeutic approach, which might be subject to further testing. Additionally, the secondary objective of this study is to determine the preliminary indicators for the efficacy of this treatment programme regarding urological symptoms, psychological and physical correlates, health-related quality of life, and healthcare utilization. The results can be used to calculate the optimal sample size for a randomized controlled trial (RCT).

Methods/design

Study design

This study will be conducted based on the principles of a 'cohort multiple randomized controlled trial' (cmRCT) proposed by Relton et al. [43]. In this pragmatic study design, an observational cohort of subjects with the parameter of interest will be recruited and evaluated on a regular basis. For a randomized controlled trial, random subjects from all eligible subjects in the cohort are allocated to the intervention group, while allocation to the control group is not randomized [43].

The feasibility study is embedded in the Interdisciplinary Research Platform Chronic Pelvic Pain Syndrome (CPPS), which was initiated in 2012 at the University Medical Center Hamburg-Eppendorf to obtain insight into the somatic and psychological aspects in CPPS and to develop treatment strategies for these patients. In cooperation with different medical specialties (e.g. psychosomatic medicine, urology, gynaecology, and physiotherapy), a specialized outpatient clinic for patients with CPPS was implemented [5]. The assessment at this outpatient clinic includes a diagnosis of CPPS according to the EAU guidelines [1]. People diagnosed with CPPS constitute the observational cohort, from which subjects for this study will be recruited.

The treatment will consist of a combination of cognitive behavioural psychotherapy and physiotherapy based on an aetiological model developed especially for patients with

CPPS [6]. Psychotherapeutic and physiotherapeutic treatment modalities will be applied as consecutive modules, and both sequences will be tested (psychotherapy followed by physiotherapy vs physiotherapy followed by psychotherapy). The intervention will therefore consist of two branches, one starting with psychotherapy and the other starting with physiotherapy. For a detailed overview of the study design, see Fig. 1.

Sample

Study subjects will be recruited from the observational cohort consisting of all patients assessed at the interdisciplinary outpatient clinic for CPPS at the University Medical Center Hamburg-Eppendorf.

The following criteria will be applied to identify eligible patients in the observational cohort: CPPS diagnosis according to the EAU guidelines [1] and classification of the International Association for the Study of Pain [44], informed consent, sufficient German language skills, age > 18 years, and score ≤ 40 for the mental or physical scale of the 12-Item Short-Form Health Survey (SF-12) [45]. Exclusion criteria are delusional disorders, substance dependence (except nicotine or pain medication), acute suicidal tendencies, planned absences over the treatment period, and current psychotherapy or physiotherapy.

The targeted sample size for the study is 54 participants. Thirty-six participants will be assigned to the intervention group and 18 to the control group. This sample size allows for evaluation of the study in terms of feasibility and can be used to estimate therapeutic effects (pre–post and between groups). Although the sample size is not sufficient to prove the efficacy of the combined treatment programme, the results of the study can be used to calculate the sample size for a subsequent RCT.

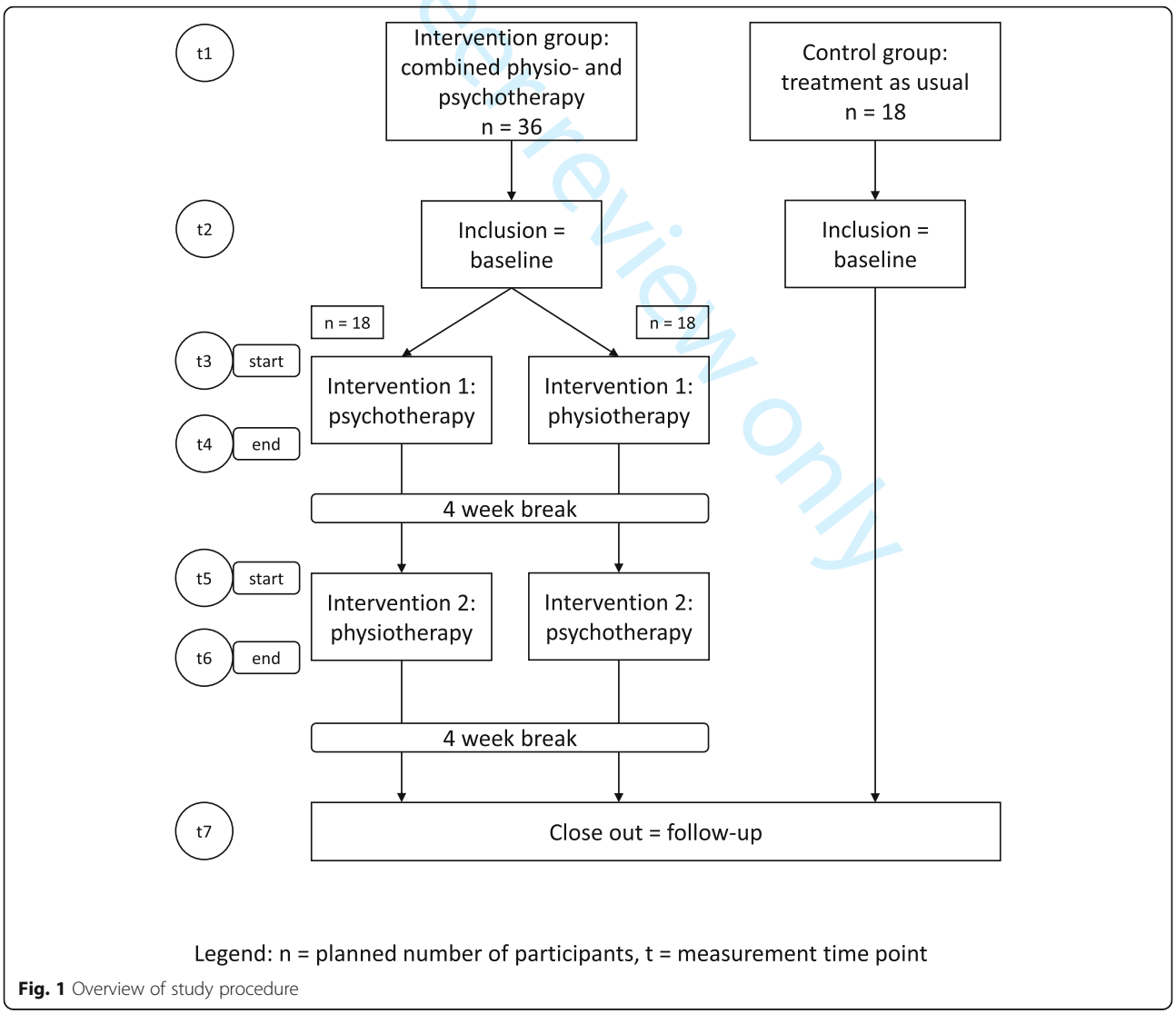

Fig. 1 Overview of study procedure

Assignment of eligible subjects to treatment and control groups will not be randomized; instead, it will be determined by the ability to regularly participate in the treatment sessions at the University Medical Center Hamburg-Eppendorf. Regular participation is defined as a maximum miss of four of the 18 treatment sessions. The assignment to one of the two treatment sequences (starting with psychotherapy vs starting with physiotherapy) will be randomized.

Procedure

In a first step, all eligible patients who were examined in the interdisciplinary CPPS outpatient clinic since 2012 (time point t1), and are thus part of the observational cohort, will be identified and assigned to either the treatment group or the control group. Detailed information about the pilot study will be sent to these patients by postal mail, whereby the informed consent signed previously by patients for the assessment at the outpatient clinic facilitates contacting them for future research. Patients willing to participate in either the treatment group or the control group will undergo a telephone interview to re-examine eligibility in case changes have occurred since their visit to the outpatient clinic and to answer open questions about the study. After inclusion, participants will receive two copies of the informed consent document, the final time schedule and a set of questionnaires (time point t2; see Instruments for a detailed description). Participants of the treatment group will also be contacted by a physiotherapist to schedule an examination appointment. Patients who do not meet inclusion criteria will be informed by telephone and will receive support regarding alternative treatment options, if requested. Patients' reasons for non-participation, if given, will be documented. In addition, patients who do not respond to the initial letter will also be contacted by telephone.

Further measurements will be conducted at the beginning (t3) and end of the first intervention module (t4) and at the beginning (t5) and the end of the second intervention module (t6) as well as 4 weeks after finishing the second intervention module (t7). The study procedure is in line with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement 2013 [46] (see also Additional file 1: SPIRIT checklist). Figure 2 displays the schedule of enrolment, interventions, and assessments according to the SPIRIT statement.

Intervention group

The intervention will consist of two consecutive treatment modules (cognitive behavioural group psychotherapy and physiotherapy as both group and individual sessions). A 4-week break is scheduled between the two modules. The intervention group has two branches; therefore, subjects will start with either one of the modules described in the following. A group size of nine patients for the psychotherapy as well as for the physiotherapy group sessions is regarded as adequate even in the event of drop-outs. This group size also reflects the maximal number of patients allowed in a CBT group in the German healthcare system [47]. The groups will be gender homogeneous because CPPS is characterized by symptoms in an intimate body region potentially associated with shame [48]. With a targeted sample size of 36 participants in the intervention and a group size of nine in the therapeutic sessions, the overall intervention group will consist of four therapeutic groups, two with only male participants and two with only female participants. One group of each gender will start with either psychotherapy or physiotherapy, resulting in four treatment groups in the intervention group.

Cognitive behavioural psychotherapy

The psychotherapeutic intervention will consist of nine weekly group sessions, each lasting 90 minutes. The sessions will be based on the following pattern: group discussion of assignments (behaviour analysis, reading a particular chapter from the patient workbook described in the following), progressive muscle relaxation (PMR) according to Jacobson [49], session-specific theory, consolidation of the specific theory through group work, concluding round, and new assignments. For a detailed overview of the CBT, see Table 1. Each session will be held by a trained and skilled CBT therapist (licensed psychotherapist) and a co-therapist (resident physician); one will be male and the other female. In order to increase generalizability we have a pool of five therapists (three female, two male) who can deliver the study intervention. All therapists will receive in-house training especially for the study and will be supervised by one specialist in CBT. During the initial session, patients will receive a printed version of the patient workbook containing theoretical background information, assignments, and repeated questionnaires regarding their symptoms for the self-evaluation of their course.

The patient workbook for cognitive behavioural group psychotherapy has been designed by members of our study group, and is based on the work of Tripp, Nickel, and Mullins [50, 51] who developed a treatment rationale for individual therapy and demonstrated its feasibility and yielded first indicators of its efficacy [35]. Through cooperation with the Canadian workgroup, we were able to translate, expand, and adapt their patient workbook [51] to the needs of our study and the German healthcare system. Key topics for the cognitive behavioural intervention are as follows:

		STUDY PERIOD					
	Outpatient clinic	Enrolment	Post-allocation				Close-out
			Start intervention 1	End intervention 1	Start intervention 2	End intervention 2	4-week follow-up
TIMEPOINT	t_1	t_2	t_3	t_4	t_5	t_6	t_7
ENROLMENT:							
Eligibility screen		X					
Informed consent		X					
Allocation		X					
INTERVENTIONS:							
Psychotherapy + Physiotherapy			←	→	←	→	
Physiotherapy + Psychotherapy			←	→	←	→	
Control group							
ASSESSMENTS:							
Sociodemographic data, case history	X						
Examination by a physical therapist	X	X			X		X
Health Care Utilization Questionnaire	X	X	X	X	X	X	X
Urological symptoms (NIH-CPSI)	X	X	X	X	X	X	X
Health-related quality of life (SF-12)	X	X	X	X	X	X	X
Pain perception (SF-MPQ)	X	X	X	X	X	X	X
Impact of pain on daily activities (PDI)	X	X	X	X	X	X	X
Catastrophizing thinking (PCS)	X	X	X	X	X	X	X
Perceived stress (PSQ)	X	X	X	X	X	X	X
Depressive symptoms (PHQ-9)	X	X	X	X	X	X	X
Somatic symptom severity (PHQ-15)	X	X	X	X	X	X	X
Generalized anxiety (GAD-7)	X	X	X	X	X	X	X
Goal attainment (GAS)*				(X)		(X)	
Patient satisfaction			X	X	X	X	

Fig. 2 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) schedule of enrolment, interventions, and assessments [46]. Legend: *GAD* = Generalized Anxiety Disorder Scale; *GAS* = Goal Attainment Scaling; *NIH-CPSI* = Chronic Prostatitis Symptom Index of the National Institute of Health; *PCS* = Pain Catastrophizing Scale; *PDI* = Pain Disability Index; *PHQ* = Patient Health Questionnaire; *PSQ* = Perceived Stress Questionnaire; *SF-MPQ* = Short-Form McGill Pain Questionnaire; *SF-12* = 12-Item Short-Form Health Survey; t = time point; * = only after the physical therapy intervention module (either at t4 or at t6)

Table 1 Overview of cognitive behavioural group psychotherapy sessions

Session	Content	Modality
1	Introduction to the programme; issuing of the patient workbook; overview of key topics; introduction to PMR	Group (90 min)
2	Group discussion/debriefing of Chapter 1 of the patient workbook; exercise of PMR; behaviour analysis	Group (90 min)
3	Group discussion/debriefing of Chapter 2 of the patient workbook; exercise of PMR; theory: catastrophizing cognitions; behaviour analysis	Group (90 min)
4	Group discussion/debriefing of Chapter 3 of the patient workbook; exercise of PMR; theory: negative self-talk; behaviour analysis	Group (90 min)
5	Group discussion/debriefing of Chapter 4 of the patient workbook; exercise of PMR; theory: influence of social relationships (Part 1); modification of 'I-message'; behaviour analysis (focus: social interaction)	Group (90 min)
6	Group discussion/debriefing of Chapter 5 of the patient workbook; exercise of PMR; theory: influence of social relationships (Part 2)/asking for support; modification of listening skills; behaviour analysis	Group (90 min)
7	Group discussion/debriefing of Chapter 6 of the patient workbook; exercise of PMR; theory: coping strategies (Part 1)/role of positive self-messages; behaviour analysis	Group (90 min)
8	Group discussion/debriefing of Chapter 7 of the patient workbook; exercise of PMR; theory: coping strategies (Part 2); activity and inactivity/recognizing avoidance behaviour; behaviour analysis	Group (90 min)
9	Group discussion/debriefing of Chapter 8 of the patient workbook; exercise of PMR; assessment of changes during the programme; revision of key topics	Group (90 min)

min minutes, *PMR* progressive muscle relaxation

- coping with catastrophizing cognitions,
- reduction of avoidance behaviour/increase of physical activity,
- development of coping strategies, and
- enhancing social support.

Furthermore, behaviour analysis also plays a key role in the programme. As group therapy facilitates the acquisition of new behaviour patterns [52], behaviour changes are addressed in the group setting. To increase the possibility of implementation into the German healthcare system we adapted the workbook to a group context.

Physiotherapy

Following the structure of the psychotherapeutic intervention, the physiotherapeutic approach is also designed in nine weekly units. However, unlike the sessions in the psychotherapy, only units 1, 5, and 9 are group treatments, while the others are designed as individual appointments. The group sessions will last 90 minutes each, and the individual sessions will last 60 minutes except for the seventh unit, which will last 90 minutes and include treatment as well as feedback and reflection about the achievement of patients' goals. Because of the more intense activity during the individual treatment and framework of ambulatory physiotherapy in the German healthcare system [53], a shorter duration was chosen in the single sessions.

The treatment is based on the Wise–Anderson Protocol, an American physiotherapeutic intervention for patients with CPPS combining trigger point therapy, a specific breathing technique, relaxation, and self-management [41, 54]. A German concept that acknowledges most of the elements of the American Wise–Anderson Protocol is Reflektorische Atemtherapie® [55, 56]. The German name of the concept is a registered trademark, and the English translation 'reflective respiratory physiotherapy' is from Zalpour [57]. This therapy aims to regulate psycho-physical coherences using the respiratory system. Specific stimuli of the connective tissue, muscles and tendons, joints, and periosteum are intended to influence the involuntary breathing and diaphragm activity. Hence, the aim is not only to improve the regulation of muscle tone and mobility, but also to affect the internal organs and pelvic floor through enhanced diaphragm mobility [58]. Positive effects of reflective respiratory physiotherapy were found in a study with patients who had chronic obstructive pulmonary disease [59].

The programme will contain the following elements [58, 60]:

- Education about the anatomy and function of the musculoskeletal system and posture with an emphasis on the pelvic floor and diaphragm, the influence of stress on the muscle tone and stiffness of fasciae, and the importance of self-management and adherence to a home exercise programme.
- Application of heat in the form of 'hot towels' (hot water-soaked towels) at the beginning of the therapy to relax muscles and joints, stimulate the circulation, and prepare the tissue for the following techniques.
- Manual techniques for all structures of the musculoskeletal system to mobilize joints and release fasciae with stretching and relaxing muscles.
- Specific therapeutic movements with partially uncomfortable or painful stimuli that influence the respiratory system and the diaphragm reflectively,

affecting the vegetative nervous system and muscle tone.
- Instruction of the patient to self-management and home exercises based on yoga to strengthen and stretch muscles, improve posture and body perception, and sense breathing activity.

In the individual sessions, subjects will be treated according to their individual findings with 'hot towels', manual techniques, and specific therapeutic movements. In addition, home exercises will be taught. During the group sessions, the focus will be on home exercises and self-management together with education and information. Similar to the psychotherapeutic group sessions, the physiotherapy group sessions will be hosted by two physiotherapists, one male and one female. Table 2 presents a scheme for the procedure and content of the physiotherapeutic intervention.

Control group

Allocation to the control group will not be randomized; instead, this will be determined by the ability to participate in the intervention occurring at the University Medical Center Hamburg-Eppendorf. It was considered difficult for patients outside the greater Hamburg area to participate; therefore, they will be allocated to the control group. The control group will not receive any specific intervention as part of the study; nonetheless, patients can seek treatment as usual from their local healthcare provider. Assessment of the control group will be done at two time points; first, at time point t2, which is the enrolment time; and second, at time point t7, which is 4 weeks after the intervention group has finished the second intervention module. The results of these measurements will be compared with the results of the intervention group to gather initial insight into the efficacy of the intervention compared to treatment as usual.

Instruments

The assessment at our interdisciplinary CPPS outpatient clinic constitutes the measurement time point t1. This involves collection of socio-demographic data and the case history, an examination by a physiotherapist, and completion of psychometric questionnaires used in this study. For an overview of the instruments used in this study, see Fig. 2.

Feasibility will be operationalized using information from the participants, therapists, and those involved in organization of the study. Information from participants will include the response rate to study invitation, willingness to participate, and reasons for not participating as indicators of demand. Practicality will be operationalized in terms of the time and personnel expenditures. Attendance at and satisfaction with physiotherapy and psychotherapy sessions, the number of drop-outs and adverse events, and the amount of missing data in the questionnaires of the workbook will function as indicators of acceptability. To assess satisfaction, we developed questionnaires using 7-point Likert scales. Subjects will be asked to rate each psychotherapeutic and physiotherapeutic session, including the accompanying study materials, each whole treatment module (psychotherapy or physiotherapy), and overall contentment with the combination of psychotherapy and physiotherapy. The questionnaires cover therapeutic and organizational aspects.

The secondary objectives of the feasibility study will be measured using the following instruments:

Table 2 Overview of physiotherapy sessions

Session	Content	Modality
1	Relationship between muscle tension, stress, and pain; awareness of tension and relaxation of the pelvic floor muscles; instruction of home exercises/self-management; goal attainment scaling	Group (90 min)
2	Reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
3	Reflection of the past sessions; reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
4	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; awareness of changes during/after session	Single (60 min)
5	Reflection of the past group session; instruction of home exercises/self-management	Group (90 min)
6	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
7	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
	Feedback for the individual sessions; evaluation of and reflection on goal attainment; self-management	Single (30 min)
8	Reflection of the past individual sessions; reflective respiratory physiotherapy; home exercises; working with the pain; awareness of changes during/after session	Single (60 min)
9	Evaluation of and reflection on goal attainment; self-management; home exercises; feedback and conclusion	Group (90 min)

min minutes

- The health-related quality of life will be assessed using the SF-12 [45], which has been demonstrated as reliable and valid in clinical and population-based samples [61, 62].
- The Chronic Prostatitis Symptom Index of the National Institute of Health (NIH-CPSI) [63] is considered the criterion standard for assessing urological symptom severity in CPPS in the EAU guidelines [1]. The German version with good psychometric properties [64] will be applied in this study. Since the original NIH-CPSI was designed for male patients, a modified version for female patients also exists [65].
- The German version [66] of the Short-Form McGill Pain Questionnaire (SF-MPQ) [67] will be used to assess pain perception.
- The impact of pain on the ability to participate in essential life activities will be measured with the Pain Disability Index (PDI) [68, 69], a valid and reliable [70] instrument.
- Pain catastrophization will be assessed with the aid of the Pain Catastrophizing Scale (PCS) [71], which has been shown to have good psychometric properties [72].
- To quantify the psychological symptom burden, three subscales of the German version of the Patient Health Questionnaire (PHQ-D) [73] with good psychometric characteristics [74–76] will be applied: the PHQ-9 for measuring depressive symptoms [77], the PHQ-15 for measuring the severity of somatic symptoms [78], and the Generalized Anxiety Disorder Scale (GAD-7) [76, 79] for measuring symptoms of generalized anxiety.
- The reliable and valid [80] German short version [81] of the Perceived Stress Questionnaire (PSQ) [82] will be used to assess subjectively experienced stress.
- Assessment of tender and trigger points in the abdominal wall, bottom, thighs, and pelvic floor is done with external and internal manual palpation. Although the reliability of manual palpation is variable [83, 84], it is essential in finding painful points in the muscles [85–87]. In female subjects, internal palpation is done via the vagina and rectum; in male subjects, internal palpation is done via the rectum. Prior to this examination, patients gave written informed consent to internal palpation.
- Participants set their individual therapy goals on the participation level of the International Classification of Functioning, Disability and Health [88] in the first physiotherapeutic group session and evaluate them in the last group treatment using the reliable and valid [89–92] Goal Attainment Scaling (GAS) [93].
- To assess healthcare utilization, we are using the Health Care Utilization Questionnaire, which is a modified version of the Client Socio-Demographic and Service Receipt Inventory—European Version [94] and was developed by the Institute of Health Economics and Health Services Research of the University Medical Center Hamburg-Eppendorf.

Data management and analysis

After completion of data collection, raw data will be entered in prepared electronic databases and merged with the electronically captured data. The accuracy of data will be checked by two independent researchers. Data saving and storage will be performed in accordance with the German regulation of Good Clinical Practice [95].

In addition to the quantitative data, feasibility will be analysed using qualitative data, such as answers to open questions in the satisfaction questionnaires and verbal information.

Descriptive statistics will be used to summarize the sample characteristics (e.g. sex, age, and symptom duration) and two-tailed independent *t*-tests will be used to test for significant differences between the intervention and control groups at enrolment (t2).

Subjects will be analysed on an intention-to-treat basis. To examine the course of the symptoms, related variables will be analysed using the pre–post point estimate comparisons, variability estimates, and 95% confidence intervals. The controlled study design allows for within-group as well as between-group comparisons. Paired-sample *t*-tests will be used for within-group comparisons, while the independent *t*-test will be used for between-group comparisons.

The significance level for all *t*-tests will be set at $p < 0.05$.

The analyses of the course of the symptom-related variables will function as estimates of the effect sizes, while effect estimates can be obtained for physiotherapy and psychotherapy separately as well as the overall effect estimates. These estimates can be used to determine the optimal sample size for a subsequent RCT with a normally distributed sample; hence, parametric tests will be applied as statistical procedures in the feasibility study. Factors influencing therapy success will also be examined.

Statistical analyses will be performed with IBM SPSS Statistics, Version 24 (IBM, Armonk, NY, USA).

Discussion

This article describes the research protocol for a controlled feasibility study of a combination of psychotherapeutic and physiotherapeutic treatments for patients with CPPS. The study will use an interdisciplinary short-term group intervention consisting of psychotherapy and physiotherapy for testing feasibility of the

combined intervention as well as providing the first indicators of efficacy.

The group assignment will be based on the ability of regular participation in the intervention which might lead to selection bias. However, we deemed regular attendance important for the positive effect of the whole intervention programme, and as the complete intervention will last 22 weeks (each intervention module has a duration of 9 weeks with a 4-week break in between) it will require a great concession in terms of time. Participants will not only have a weekly appointment at University Medical Center Hamburg-Eppendorf, they will also have to prepare the psychotherapeutic sessions by reading the workbook chapters and completing the respective questionnaires. It is unclear whether patients will comply with these requirements so that they will be prepared enough to follow and understand the content of the single psychotherapeutic sessions. Moreover, it is expected that at least some subjects will miss one or more sessions due to shift work, unplanned vacations, or other reasons. This might result in difficulties in understanding the content of the subsequent sessions, influencing the effect of the intervention. However, the subjects will have manuals for both the psychotherapy and physiotherapy components, which will allow them to educate themselves even if they have missed a session. Both intervention modules will be applied in a subsequent order rather than to deliver physiotherapy and psychotherapy at the same time. This approach was chosen so that participants have to make time for a weekly appointment and estimate the effects of each module separately. Nonetheless, some patients might find it tempting to select the intervention module they find more interesting or suitable for their individual situation and skip the other one. In addition, the subsequent order contributes to the prolongation of the overall treatment period. All psychotherapy sessions will be provided as group treatments. Group sessions will be accompanied by a workbook, which requires that participants adhere to specific assignments and may influence their motivation. Nonetheless, the workbook provides support and advice both during the intervention period and after its completion.

Prior studies suggest that physiotherapy is highly valued by patients with CPPS [6, 96] and can empower them to take responsibility for themselves and their coping with pain [97]. During the design of the intervention, the aspect of empowerment and self-management was emphasized, which was a strength of the study. Moreover, instead of adapting a foreign concept such as the Wise–Anderson Protocol [54], a German, already implemented, physiotherapeutic management approach was used. The combination of physiotherapeutic group and individual sessions is not part of the regular health care in ambulatory settings in Germany and might be unexpected for some participants. While they will be in a confidential setting during individual treatments with the physiotherapist, they will have to cope with several other patients being present during performance of exercises. Nevertheless, this group experience can also have a positive effect on the subjects.

We intend to recruit patients from the CPPS outpatient clinic, which has been ongoing since 2012 and serves as the observational cohort in our study design. This cohort is limited in size, and it could be brought into question whether sufficient patients are willing to participate and fulfil eligibility criteria. Their initial assessment at the outpatient clinic might be several months to years prior and their situation with regard, but non-exclusive, to the CPPS might have changed, resulting in non-participation in the study. However, this feasibility study should provide information for further optimization of the treatment approach and power calculation in future RCTs rather than sufficient testing of programme effects. Because of the exploratory nature of the study, no sample calculation was performed, and the selection of controls was based on pragmatic reasons. Nevertheless, to the authors' knowledge, this study is the first to evaluate a combined programme of psychotherapy and physiotherapy for patients with CPPS while acknowledging the multifactorial aetiology and demand for multimodal therapies [1, 17].

Trial status

The study is currently ongoing. Recruitment of patients started in mid-May 2016 and will continue until the targeted sample size is reached. The first two groups, one that started with physiotherapy and the other with psychotherapy, underwent treatment from June to November 2016. The second two groups started in January 2017 and will be treated until June 2017. The next two groups are supposed to start treatment in July 2017.

Additional file

Additional file 1: Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist (DOC 120 kb)

Abbreviations

CBT: Cognitive behavioural therapy; cmRCT: Cohort multiple randomized controlled trial; CPPS: Chronic Pelvic Pain Syndrome; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders IV; EAU: European Association of Urology; GAD-7: Generalized Anxiety Disorder Scale; GAS: Goal Attainment Scaling; NIH-CPSI: Chronic Prostatitis Symptom Index of the National Institute of Health; PCS: Pain Catastrophizing Scale; PDI: Pain Disability Index; PHQ: Patient Health Questionnaire; PMR: Progressive muscle relaxation; PSQ: Perceived Stress Questionnaire; RCT: Randomized controlled trial; SCID: Structured Clinical Interview for DSM-IV Axis I Disorders; SF-12: 12-Item Short-Form Health Survey; SF-MPQ: Short-Form McGill Pain Questionnaire

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Availability of data and materials
The datasets which will be generated during the current study will be available from the corresponding author on reasonable request.

Participants' safety and adverse events
Participants will be covered by the patient insurance of the University Medical Center Hamburg-Eppendorf. Both the psychotherapy and the physiotherapy will be conducted by health professionals trained specifically and knowledgeable in safe application as well as appraisal of the therapy modalities. However, in case of any adverse event, medical care is available at any time through the University Medical Center Hamburg-Eppendorf. All adverse events will be documented and serious adverse events will be reported to the ethics committee within one working day.

Authors' contributions
CAB is responsible for study design, project management, and editing of the manuscript. SGRK is responsible for writing of the manuscript. CD is responsible for critical revision of the manuscript. BR is responsible for study design and critical revision of the manuscript. SG is responsible for writing of the manuscript. DAT is responsible for preliminary work in the design of the psychotherapeutic treatment rationale and patient workbook. GK is responsible for study design, project management, and editing of the manuscript. BL is responsible for study design, project management, supervision of the study, and editing of the manuscript. All authors commented on the draft and approved the final manuscript.

Ethics approval and consent to participate
The study protocol has been conducted according to the Declaration of Helsinki and has been approved by the Ethics Committee of the Medical Association Hamburg, Germany (2 December 2014; reference number PV4801). Patients, who were contacted during recruitment, have given their consent to be contacted in the future during the initial examination at the CPPS outpatient clinic (which has been approved by the Ethics Committee of the Medical Association Hamburg, Germany; 17 August 2012; reference number PV4220). Patients participating in the feasibility study will sign a separate informed consent form that has been approved by the ethics committee. The informed consent in duplicate will be send to the participants by mail.

Consent for publication
Not applicable.

Competing interests
GK declares that she is a co-founder of the Association for Reflective Respiratory Physiotherapy (Verein für Reflektorische Atemtherapie e.V.), which was established in 2000. She has been a freelance lecturer for reflective respiratory physiotherapy for over 15 years. The other authors declare that they have no competing interests.

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